OFFICE OF TOXIC SUBSTANCES

REV. 7/27/82

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Reports O - 5 File

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GENERAL ELECTRIC

GENERAL ELECTRIC COMPANY

FAIRFIELD, CONNECTICUT 06431

JAMES R. DONNALLEY
VICE PRESIDENT
CORPORATE ENVIRONMENTAL ISSUES PROJECT
CORPORATE TECHNOLOGY STAFF

February 25, 1982

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Documents Control Officer (TS-793)
Office of Pesticides & Toxic Substances
Environmental Protection Agency
Room E-401
401 M Street, S.W.
Washington, DC 20460

Re: Docket Number OPTS-62017 & 62018

Dear Sir:

On behalf of the General Electric Company, I enclose three (3) copies of "Studies of Employees Occupationally Exposed to PCBs," a progress report by Dr. Richard W. Lawton, et al. of GE's Corporate Research & Development organization. This report covers much of the work GE has done so far in following its capacitor manufacturing employees exposed to PCBs prior to 1977.

It should be emphasized that this is an interim report, not a finished project. We are nonetheless making this report available to EPA now in the hope it will prove a helpful addition to the above dockets.

We intend to publish this work once we have completed our interpretation of the data. The main area of further work is in the quantification of the PCB serum levels. While we have made analyses by the current best "state of the art" approach, we believe that the method overstates actual levels quite significantly. We are evaluating alternative ways of analyzing the data before we finalize our report.

Very truly yours,

J R Donnalley

fm
enclosures

cc: Dr. John Todhunter

'54

65-8250450

STUDIES OF EMPLOYEES
OCCUPATIONALLY EXPOSED TO PCBs

A Progress Report
by

Richard W. Lawton, M.D. (1)
Barbara T. Sack, B.S. (1)
Marie R. Ross, R.N., C.O.H.N. (2)
Joseph Feingold, M.D. (2)

with editorial assistance from

John F. Brown, Jr., PhD (1)
John A. Bergeron, PhD (1)

(1) General Electric Research and Development Center
P.O. Box 8, Schenectady, N.Y. 12301

(2) General Electric Capacitor Products Dept.
John St., Hudson Falls, N.Y. 12839

September 18, 1981

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1. INTRODUCTION

Between 1975 and 1976, General Electric Company initiated both a continuing industrial hygiene survey to determine the actual PCB levels at a number of points in and around its Hudson Falls and Fort Edward capacitor plants, and a medical study of some of the employees at those plants (initially, 194 persons) believed to be among the employees most heavily exposed to PCBs. The scope of both the industrial hygiene and medical surveillance programs was enlarged in 1979 to provide data required for more elaborate analyses.

This report responds to requests for preliminary data and documentation on the two programs. The 13 areas of scientific concern are described in individual sections, as opposed to grouping corresponding elements of each area under broader categories (methods, results, conclusions, etc.) appropriate for a final report. Information contained herein is subject to change and/or qualification.

2. Descriptions of Plants, Products, Processes and PCBs Used

The use of polychlorinated biphenyls (originally, pentachlorobiphenyl) in ordinary foil-and-paper capacitors was initiated by General Electric in 1930. PCBs soon superseded previously used dielectric fluids in all but a few specialty applications. From 1946 through 1977, all General Electric manufacture of PCB capacitors was carried out in eastern upstate New York in its Hudson Falls and Fort Edward plants.

The major manufacturing operations used at the Hudson Falls and Fort Edward plants are listed in Table 2-1. Of these operations, only three - prefiltering of the impregnant, impregnation and sealing of the capacitors merit further description at this time.

TABLE 2-1

MANUFACTURING OPERATIONS ASSOCIATED WITH
CAPACITOR PRODUCTION AT HUDSON FALLS AND FORT EDWARD PLANTS

Operation	Hudson Falls Plant	Fort Edward Plant
1. Rolling of aluminum ingots into sheets which are subsequently employed as capacitor plates and cans		X
2. Fabrication of capacitor plates, brackets and cans from sheet aluminum and steel	X	
3. Capacitor component washing		
a. Ultrasonic cleaning	X	
b. Vapor degreasing	X	X
4. Rolling of capacitor plates with spacer paper	X	X
5. Assembly of capacitor components	X	X
6. Vacuum drying of capacitor prior to impregnation with oil	X	X
7. Prefiltering of impregnant	X	X
8. Impregnation of the capacitors with any of various oils (including PCB, DOP, mineral oil, castor oil)		
a. Vacuum flood fill	X	X
b. Individual vacuum fill	X	
9. Cleaning of the exteriors of the filled capacitors		
a. Detergent water wash		X
b. Vapor degreasing	X	
10. Pretreatment of the exteriors of the filled capacitors prior to painting		
a. Iron phosphate or fluoride wash		X
b. Vapor degreasing	X	
11. Painting of the exteriors of the capacitors	X	X
12. Packaging, storing and shipping of the finished product	X	X

"Prefiltering of impregnant" was an operation performed upon all dielectric fluids used in the plant, including both new and recycled PCBs. It consisted of percolating the fluid through a bed of Florida clay (fuller's earth) for the removal of polar impurities, which would contribute to dielectric loss if present. An additional benefit, unrecognized at the time, was that such treatment may have reduced the levels of polychlorinated dibenzofurans (PCDFs), if present, as contaminants in the PCBs.

"Impregnation of the capacitors" consisted of admitting warm dielectric fluid to the vacuum-dried capacitor under vacuum, to enable complete filling of the entire structure (no air bubbles). Impregnation procedures varied with capacitor size. Large capacitors (those requiring up to several gallons of dielectric fluid) were originally filled manually through ports in their tops, an operation that resulted in spillage and dermal contact. In the mid-1960's this was decreased considerably when an automated manifolded filling system, under electronic control, was developed. Small capacitors (which typically require only a few milliliters of dielectric fluid) were impregnated by flooding with the dielectric fluid under vacuum in large ovens.

Following impregnation, the racks of warm, wet, small capacitors were transported on dollys by "movemen" to the "sealing" station where the filling ports were soldered shut. They were then taken to a washing station for the removal of the fluid from their outer surfaces.

The salvage and repair of large capacitors that did not meet test specifications, an operation not included in Table 2-1, involved drilling for drainage of the PCB, milling off the cover seal, and manually removing and repairing the wet components.

As a result of volatilization, condensation, dripping and spillage, the capacitor impregnation, sealing and salvage operations created local environments where significant portions of all exposed surfaces were wet with PCBs, and where air levels in the immediate vicinity of such surfaces could become saturated with PCB vapor. There were considerable opportunities for both dermal and respiratory uptake among individuals performing jobs related to these manufacturing operations, and also opportunities for respiratory uptake among those working at other operations that happened to be located nearby in the plant. Physical lay-outs of the plants changed repeatedly, and records of many of the lay-outs are unavailable. Thus, it is not possible to identify other manufacturing operations which might have resulted in unusually high exposures to PCBs because of physical proximity to the impregnation, sealing or salvage activities.

Table 2-2 presents the available information on the composition of dielectric fluids used at the Hudson Falls - Fort Edward plants. The initial (1940's) production of PCB capacitors used Aroclor 1254, a commercial mixture of chlorinated biphenyl homologs and isomers having the average molecular composition of a pentachlorobiphenyl. In the 1950's, Aroclor 1254 was replaced in most capacitor lines by Aroclor 1242 (a chlorinated biphenyl mixture having the average composition of a trichlorobiphenyl). In 1971, Aroclor 1242 was replaced by Aroclor 1016, a material that also had the average composition of a trichlorobiphenyl, but which had been redistilled to remove all homologs containing more than four chlorines per biphenyl. On June 30, 1977, all PCB usage ceased.

TABLE 2-2. Available Data on Usage of PCB-Based Dielectric Fluids in Hudson Falls (HF) and Ft. Edward (FE) Plants and Temperatures of Exposure to Plant Environment.

Year	Plant	Pyranol Grade	% of Production	Composition (see Key)
1946	FE	1476	95	100% 1254
		1436	4	75% 1254, 25% TCB, 1% BCA
		1481	1	75% 1254, 25% TCB
1950	FE	1499	80	100% 1242
		1476	15	100% 1254
		1436	4	75% 1254, 25% TCB, 1% BCA
		1481	1	75% 1254, 25% TCB
1952	HF	1476	95	100% 1254
		1436	4	75% 1254. 25% TCB, 1% BCA
		1481	1	75% 1254, 25% TCB
1953	HF	1499	~25	100% 1242
		1476	~70	100% 1254
		1436	4	75% 1254, etc.
		1481	1	75% 1254, etc.
1955	HF, FE	1499	95	100% 1242
		1436	5	75% 1254, etc
1956-59 - Unconfirmed report of switch back to 1254				
1964	HF, FE	PII	99	100% 1242, 0.35% 4206
		1436	1	75% 1254, etc.
1965	HF, FE	PII	99	99% 1242, 0.7% 4221
		1436	1	75% 1254, etc.
1971	HF, FE	PII	99	99% 1016
		1436	1	75% 1254, etc.
1975	- Report of reintroduction of 0.7% 4221			
1976	- Displacement of 1016 by DEHP commenced			
1977	HF, FE	PII	25%	99% 1016, 0.7% 4221
1977	- June 30 - All PCB usage discontinued			

Temperatures at Which Wet Units Exposed to Air

Aroclor 1254-based fluids,	FE,	90-95°C
" " " "	HF,	45-60°C
Aroclor 1242 or 1016 fluids	FE,	65-70°C
" " " "	HF,	45-60°C

Key: 1254, Monsanto Aroclor 1254, pentachlorobiphenyl mixture. 1242, Monsanto Aroclor 1242, trichlorobiphenyl mixture. 1016, Monsanto Aroclor 1016, trichlorobiphenyl mixture redistilled to remove penta- and higher chlorobiphenyls. TCB, trichlorobenzene mixture. BCA, betachloroanthraquinone. 4206, Union Carbide epoxide 4206, 4-vinylcyclohexene diepoxide. 4221, Union Carbide epoxide 4221, 3,4-epoxy-6-methylcyclohexylmethyl 3,4-epoxy-6-methylcyclohexane carboxylate. DEHP, di(2-ethylhexyl) phthalate.

Data courtesy of Earl Dunham, GE Capacitor Products Dept.

Table 2-2 indicates that the mixtures put into the capacitors contained about 0.5% of epoxide stabilizers and sometimes trichlorobenzene as well. Stabilizer 4206 was abandoned in favor of 4221 because of some cases of contact dermatitis, the cause of which was identified by State health officials. In addition, there were opportunities for exposure to dusts, oils, solvents and heavy metals at certain zones in the plants.

Available analytical data indicate that PCDFs were present only at toxicologically insignificant levels (0-2 ppm) in specimens of Aroclor 1254, 1242 and 1016 manufactured in the 1970's. It is not presently known what levels may have been present in specimens made during earlier periods, nor to what extent such levels may have been reduced by the "prefiltering" operation. To resolve these questions, datable GE capacitors manufactured over the entire 1946-1977 period are being collected and will be analyzed for PCDFs as soon as the necessary instrumentation becomes operational.

3. PCB Air Levels in Plant and Surrounding Areas

In order to determine levels of PCBs in the air within and around the plant, air samples were collected by various General Electric industrial hygienists in 1975, 1977, 1978 and 1980; by NIOSH in 1977; and by the State of New York between 1976 and 1980. The initial Company samplings used toluene and hexane as collection media; all subsequent samplings used florisil. The NIOSH investigators collected both personal and area air samples; all of the other investigators collected area samples only. In most cases, the PCBs recovered from the collection media were injected directly into a gas chromatograph, and PCB levels determined by comparing gas chromatographic peak heights with those of an Aroclor 1242 standard.

However, in the Company's 1980 study two alternatives were also examined: use of an Aroclor 1016 standard and perchlorination of the removed PCB mixture, followed by gas chromatographic quantitation as the single species decachlorobiphenyl. Most of the observations reported by these various surveys of PCB air levels are listed in Tables 3-1 through 3-12, or indicated by the individual data points on Figure 3-1 (below).

As is characteristic of environmental sampling data, considerable variations in point-to-point PCB levels were observed within the plant, and also considerable variations between successive measurements made at the same point at different times, the latter being particularly marked for the PCB measurements made in the surrounding community. (Tables 3-9, 3-10, 3-11, 3-12 and Fig. 3-1). Such data is frequently found to be log-normally distributed, however; and this was observed to be the case for the PCB sampling data as well. Figure 3-2 shows the total data from Tables 3-1, 3-2, 3-3, 3-8 and 3-9 (upper half) plotted as log (PCBs) versus percentile ranking on probability paper, demonstrating the linear relationships expected for log-normally distributed data. Similar relationships were also observed for the other data sets as well (plots not shown.) As a result, it was possible to summarize the information contained in these data sets in terms of geometric means (equivalent to medians) and log (standard deviation). Such summary data, along with the somewhat less informative data on arithmetic means and coefficients of variation, are given for the various GE in-plant sampling studies in Table 3-13, and for the NIOSH in-plant sampling in Table 3-14. The overall trends in geometric mean PCB levels within the two plants, and at the State monitoring station (on the top of the Washington County Office

TABLE 3-1

CONCENTRATION OF POLYCHLORINATED BIPHENYL FOUND AT
GENERAL ELECTRIC-CPD-HUDSON FALLS - 10/23-24/75

AREA AIR SAMPLES   Collection Media: Nana Grade Toluene

STATIONS	CONCENTRATION μg/m³
Manifold Fill (Oper Position)	480
Manifold Fill (Solder Closure)	1040
Manifold Fill (Test & Leak Repair)	260
Treat Tank Tub (Unloading)	911
Treat Tank Tub (Closure)	295
Repair Area (Mill Oper)	609
Repair Area (Mill Oper Drain)	1060
Repair Area (Controlled Envir. Room)	680

STATIONS	CONCENTRATION μg/m³
Repair Area (Weld or Solder Closure)	1160
Heat Sink (Normal Oper)	660
Heat Sink (Leaker)	832
Building 9-2 (Salvage Drain)	390
Building 9-2 (Salvage Dis & Reassemble)	830
Building 10 (Inst Lab - 2nd Floor)	644
Building 10 (Office Area)	260

Sample Duration: 90 - 400 min.
Sample Volume: 29 - 110 liters

TABLE 3-2

CONCENTRATION OF POLYCHLORINATED BIPHENYL FOUND AT
GENERAL ELECTRIC-CPD-FT. EDWARD - 10/23-25/75

AREA AIR SAMPLES   Collection Media: Nano Grade Toluene

STATIONS	CONCENTRATION $\mu g/m^3$	STATIONS	CONCENTRATION $\mu g/m^3$
Carousel #2 (Oper Pos.)	548	CEB Crimp Station (Left)	954
Carousel #2 (Tilt)	586	CEB (Washer Ent.)	795
Carousel #2 (Bldg. 23 Conv.)	360	CEB (Accumulation)	1590
Carousel #2 (El. Cage at Rear)	450	Mid Room Treat	408
Carousel #2 (Solder Station)	675	Refinery Room	500
Carousel #2 (Solder Station Left)	523	Carousel #1 (Oper. Pos.)	1920
Carousel #2 (Washer Ent.)	611	Carousel #1 (Tilt)	2000
CEB Crimp Station (Right)	1560		

Sample Duration: 60 - 385 min.
Sample Volume: 21 - 97 liters

TABLE 3-3

CONCENTRATION OF POLYCHLORINATED BIPHENYL FOUND AT
GENERAL ELECTRIC-CPD-HUDSON FALLS/FT. EDWARD - 4/27/77

AREA SAMPLES

Collection Media: Nana Grade Hexcne

FT. EDWARD STATION	CONCENTRATION µg/m³	HUDSON FALLS STATION	CONCENTRATION µg/m³
Carousel #2 (Oper. Pos)	310	Manifold Fill (Leak & Repair)	576
Carousel #2 (Solder Seal	263	Manifold Fill (Oper Pos)	273
Carousel #2 (Washer Ent)	330	Manifold Fill (Solder Closure)	582
Carousel #2 (Collection Area)	496	Repair Area (Mill Oper)	251
Carousel #2 (Auto Trait)	176	Repair Area (Drain)	369
Refinery Room	172	Repair Area (Weld and Solder Closure)	230
Carousel #1 (Oper Pos)	417	Heat Sink (Leaker)	227
Carousel #1 (Tilt)	365	Building 9-2 (Salvage and Reassemble)	260

Sample Duration: 74 - 416 min
Sample Volume: 37 - 244 liters

000014

TABLE 3-4

NIOSH SITE AUDIT

CONCENTRATIONS OF POLYCHLORINATED BIPHENYLS FOUND AT THE
GENERAL ELECTRIC FACILITY IN HUDSON FALLS, NEW YORK, ON APRIL 27-28, 1977

PERSONAL AIR SAMPLES

Collecting Media: Florisil

Job Title	Date	Total Sampling Time (min.)	Total Volume (liters)	Concentration μg/m³
Treat Operator	4/27	427	82.3	55
" "	4/28	304	56.2	81
Treat Helper	4/27	426	67.0	75
" "	4/28	441	95.1	84
Recovery & Repair	4/27	422	84.5	281
" "	4/28	418	80.9	316
Repair & Seal	4/27	119*	23.8	201
" "	4/28	254*	50.9	136
EMF Operator	4/27	431	65.3	115
" "	4/28	176*	35.2	171
Repair	4/27	422	89.0	50
Salvage Operator	4/28	42[illegible]	31.0	155

*Based on known sample volume and approximate flow rate

Source: NIOSH Audit
M. Jones

000015

TABLE 3-5

HUDSON FALLS - 4/27-28/77

AREA AIR SAMPLES

NIOSH SITE AUDIT

Collecting Media: Florisil

Location	Date	Total Sampling Time (min.)	Total Volume (liters)	Concentration µg/m³
Winding	4/27	195*	38.9	43
"	4/28	420	62.9	3
Test & Paint	4/27	423	75.1	52
" "	4/28	417	84.7	30
Assembly	4/27	426	84.1	33
"	4/28	425	86.2	24
Shipping	4/27	426	82.7	16
Storage	4/28	427	85.2	14

SOURCE: NIOSH Audit
M. Jones

TABLE 3-6

CON̲CENTRATIONS OF POLYCHLORINATED BIPHENYS FOUND AT THE GENERAL ELECTRIC FACILTY IN FT. EDWARD, NEW YORK ON APRIL 27-28, 1977

PERSONAL AIR SAMPLES

NIOSH SITE AUDIT

Collecting Media: Florisil

Job Title	Date	Total Sampling Time (min.)	Total Volume (liters)	Concentration $\mu g/m^3$
Treat Operator	4/27	414	100.4	116
" "	4/28	431	28.1	203
Maintenance	4/27	404	82.7	150
Tester	4/28	440	63.8	264
"	4/27	427	83.6	226
"	4/27	423	83.5	161
Packer	4/28	434	57.1	256
"	4/27	428	81.9	166
"	4/27	425	69.3	175
Rework & Final Assem.	4/27	411	94.3	130
" " "	4/27	413	79.5	174
Rework Packer	4/28	435	60.9	132
Rework Tester	4/28	433	53.1	140
Rework & Tester Solder	4/28	271	38.7	241
Moveman (Testing & Soldering)	4/28	439	56.6	303
" "	4/27	415	84.7	173
" "	4/28	452	24.5	183
Moveman (Sealing)	4/28	432	24.3	396
"	4/27	257	51.5	389

SOURCE: NIOSH Audit
M. Jones

TABLE 3-7

FT. EDWARD - 4/27-28/77

AREA AIR SAMPLES

NIOSH SITE AUDIT

Collecting Media: Florisil

Location	Date	Total Sampling Time (min.)	Total Volume (liters)	Concentration $\mu g/m^3$
Final Assembly	4/28	423	83.9	111
" "	4/28	410*	82.0	134
" "	4/27	404	82.2	119
Soldering	4/28	398	58.2	392
"	4/27	384	53.9	564
Winding	4/28	441	63.8	54
"	4/27	387	75.1	53
Shipping	4/28	428	61.6	101
"	4/28	410	81.1	9
Can Mfg.	4/28	437	78.7	36
" "	4/27	399	82.3	67
Cover Mfg.	4/28	442	72.6	62
" "	4/27	392	75.1	25

SOURCE: NIOSH Audit
M. Jones

000018

TABLE 3-8

RESIDUAL AIRBORNE CONCENTRATIONS OF POLYCHLORINATED BIPHENYLS FOUND AT THE GENERAL ELECTRIC FACILITY - HUDSON FALLS, N.Y.

Collection Media: Florisil   Date: 3-7/78   Active PCB Use: Mid 1977

AIRBORNE PCB		STRUCTURAL PCB LEVELS	
Sample Location	μg/m³	Structure Type	ppm
Bldg. 8-2 Office	14		
Bldg. 8-2 Storage	94.9	Floor	1,400
Bldg. 8-2 Cafeteria	76.6		
Bldg. 9-2 Storage	19.1		
Bldg. 9-2 Salvage	30.9		
	389.3		
	642.5		
Bldg. 9-2 Salvage *	110		
Bldg. 10-4 Lab - Test Area	57.3		
Bldg. 104 Pilot Lab	106.0	Floor	480
		Wall	53
Bldg. 10-1 Maint. Office	65.4		
Bldg. 1-1 Teardown	206.7	Floor	1,200
Bldg. 1-1 Treat Area	158.1	Trench Area-West	3,500
	170.0	Trench Area-East	1,300
		Floor	38
Bldg. 1-1 EMF Fill (South)	41.6		
(North)	222.4	Floor	14,000
Bldg. 1-2 Shipping	4.7		
Bldg. 1-2 Tank Farm	39.8		
Bldg. 2 Refinery Area	56.5		

* Taken after washing and painting the walls of the Salvage Area

Dilution Rates Necessary to Meet Proposed Std.

Sample Location	Concentration	cfm
Bldg. 1-1 Tear Down	206.7 μg/m³	320,000
Bldg. 9-2 Salvage	642 μg/m³	400,000

Data Supplied by: D. Deeds

TABLE 3-9

RESIDUAL AIRBORNE CONCENTRATIONS OF POLYCHLORINATED BIPHENYLS FOUND AT THE GENERAL ELECTRIC FACILITY - FT. EDWARD, N.Y.

Collection Media: Florisil   Date: 3-7/78   Active PCB Use: Mid 1977

Sample Location	$\mu g/m^3$
Film Lab - 3rd Floor	48.9
	40.7
Film Storage	27.2
Tank Farm	69.7
	31.4
Maintenance Office	29.5
Bldg. 27 Solder Seal	29.6
	25.2
Bldg. 27 Carosel #2	43.3
Bldg. 23 Carosel #1	33.9
Bldg. 23 Treat	64.7
Bldg. 23 QC Lab	135.4
Bldg. 23 Accumulation & Seal	58.2

Outdoor Ambient
Airborne PCB at Hudson Falls/Ft. Edward

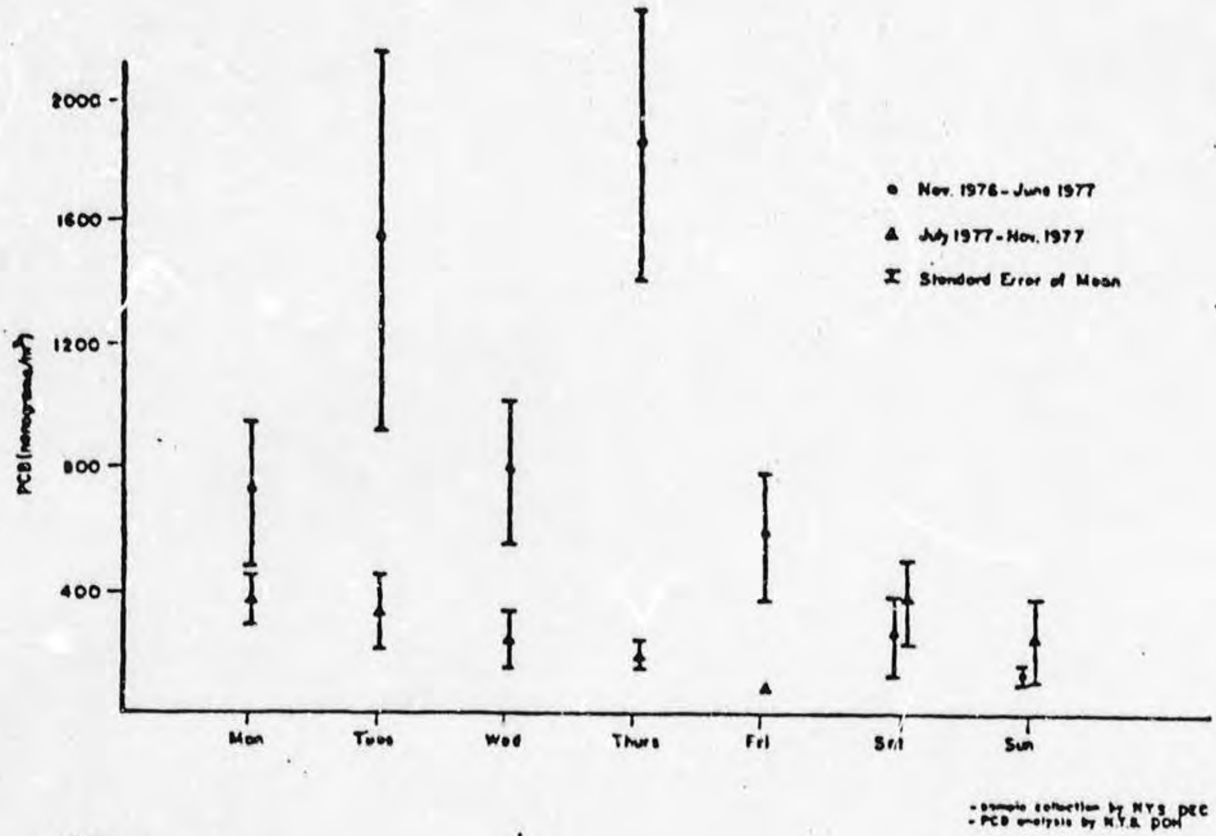
Collection Media: Florisil   Date: 8/78   Active PCB Use: Mid 1977

Sample Location	$\mu g/m^3$
Bldg. 1 Roof, Riverside	2.0
Bldg. 1 Roof	4.4
Near Bldg. 6 outside	32
Near Old Tanker Dock	4.2
Parking Lot across from Bldg. 10	1.5
D. Deeds' Yard	47
D. Deeds' Yard	1.0
Near Guard House	.94
F.E. Roof Intake Treat	1.3
F.E. Roof Intake	.15
F.E. Ground Level Behind Plant	31
Bldg. 9-2 Salvage	1.1×10^2
Bldg. 9-2 Salvage	1.1×10^2

Data Supplied By: D. Deeds

TABLE 3-10

PCB CONCENTRATIONS IN AMBIENT AIR AT WASHINGTON COUNTY OFFICES
BY DAY OF WEEK



1000 ng = 1 μg

Table 3-11: Ambient air PCB levels (ng/m³ of Aroclor 1016) at dump and dredge spoil areas.

	Caputo*	Fort Miller*	New Moreau**
	3000	4400	160
	5900†	1160	50
	4100†	930	110
	1000†		
	2200[1]		
Average:	3240	2160	107

Source: Romano[21]; PCB analysis by N.Y. Department of Health.
† These are 2.5 hr. air samples from one day. All others are 8 hr. samples.
* Dump area.
**Dredge spoil area.

TABLE 3-11
PCBs SAMPLING - FORT EDWARD

FIELD NO.	LOCATION	PCB DETECTED (µg/m³)	PCB (1016), µg/m³ (Front + back)
1180F-F-1	Tank farm, East side	86.85	71
1180F-F-2	Tank farm, West side	13.46	11
1180F-F-3	Tank farm South	10.25	12
1180F-F-4	North end tank farm	27.35	19
1180F-F-5	Carosel #1-East side	3.55	15
1180F-F-6	Carosel #1-South side	8.92	6.5
1180F-F-7	Carosel #1-West side	8.11	8.3
1180F-F-8	Treat area (middle) tank 9A10	95.91	80
1180F-F-9	QC Lab, West end	121.08	52
1180F-F-10	QC Lab, East end	247.14	130
1180F-F-11	Seal Station North	10.14	42
1180F-F-12	Treat Station North	74.90	230
1180F-F-13	Seal Station South	23.33	18
1180F-F-14	Treat Station South	38.81	41
1180F-F-15	Carosel #2 West	9.07	20
1180F-F-16	Carosel #2 East	70.00	47
1180F-F-17	Pretest & Assembly middle, West wall	47.76 *	39 *
1180F-F-18	Accumulation, South	130.21	94
1180F-F-19	Pretest & Assembly North, West wall	34.49 *	23 *
1180F-F-20	Pretest & Assembly South, West wall	34.46 *	18 *
1180F-F-21	Carosel #2 North	29.35	16

Table 3-12 PCBs Sampling - Hudson Falls 1980

FIELD NO.	LOCATION	PCB DETECTED (μg/m3)	PCB DETECTED (μg/m3)	DIRECT*	PERCHLOR	PCB (1016), μg/m3 (front + back)
1180H-F-1	EMF Fill, South	62.46		55.22	100	54
1180H-F-2	EMF Fill, Repair Room	63.98		64.64	168.1	59
1180H-F-3	EMF Fill, North	90.64		93.75	197.5	79
1180H-F-4	Treat Tanks, North Center (#22)	49.08		43.70	78.3	34
1180H-F-5	Treat Tanks, North Center (Between #11 & 12)	24.34		23.53	51.8	23
1180H-F-6	Treat Tanks, East (#16)	103.88		116.41	338.6	86
1180H-F-7	Tank Farm, South (Between #22 &23)	13.33		15.66	30.1	13
1180H-F-8	Treat Tanks, South	126.57		Blank	Blank	110
1180H-F-9	Shipping, Southwest	5.82		8.21	15.8	6.8
1180H-F-10	Shipping, North	5.08		5.71	11.4	6.9
1180H-F-11	Center, East of Tank #15	9.71		13.08	23.1	8.6
1180H-F-12	Center, West of Tank #11	15.42		16.91	32.4	18
1180H-F-13	Tank Farm, North (Between #20 & 21)	39.06		33.19	95.6	31
1180H-F-14	Refinery, South	20.53		24.13	45.6	23
1180H-F-15	Refinery, North	26.83		24.23	44.9	14
1180H-F-16	Cafeteria, East	24.27		22.76	48.3	22
1180H-F-17	Cafeteria, East	28.31		28.68	56.6	22
1180H-F-18	Repair & Recovery, West	87.89		74.54	188.6	5.1
1180H-F-19	Repair & Recovery, Center South	68.90		66.35	157.7	68
1180H-F-20	Repair & Recovery, Center North	59.82		69.46	146.0	3.[illegible]
1180H-F-21	Repair & Recovery, East	58.26		61.75	162.5	20
1180H-F-22	Bldg. 10 - Clean Room	0.69		NA	<1.15	3.6
1180H-F-23	Bldg. 10 - Room 4	16.25		NA	38.4	19
1180H-F 24	Bldg. 10 - Develop Treat Lab	20.79		NA	51.48	24
1180H-F-25	Bldg. 10 - Pilot Test	16.36		NA	70.54	19
1180H-F-26	Bldg. 10 - Basement Maintenance Office	23.62		NA	63.67	26
1180H-F-27	Bldg. 3 - Foreman's office	17.92		NA	26.09	4.3

20

0000023

000024

Figure 3-1 Air PCB Levels Observed on Roof of Washington County Office Building, Ft. Edward, NY

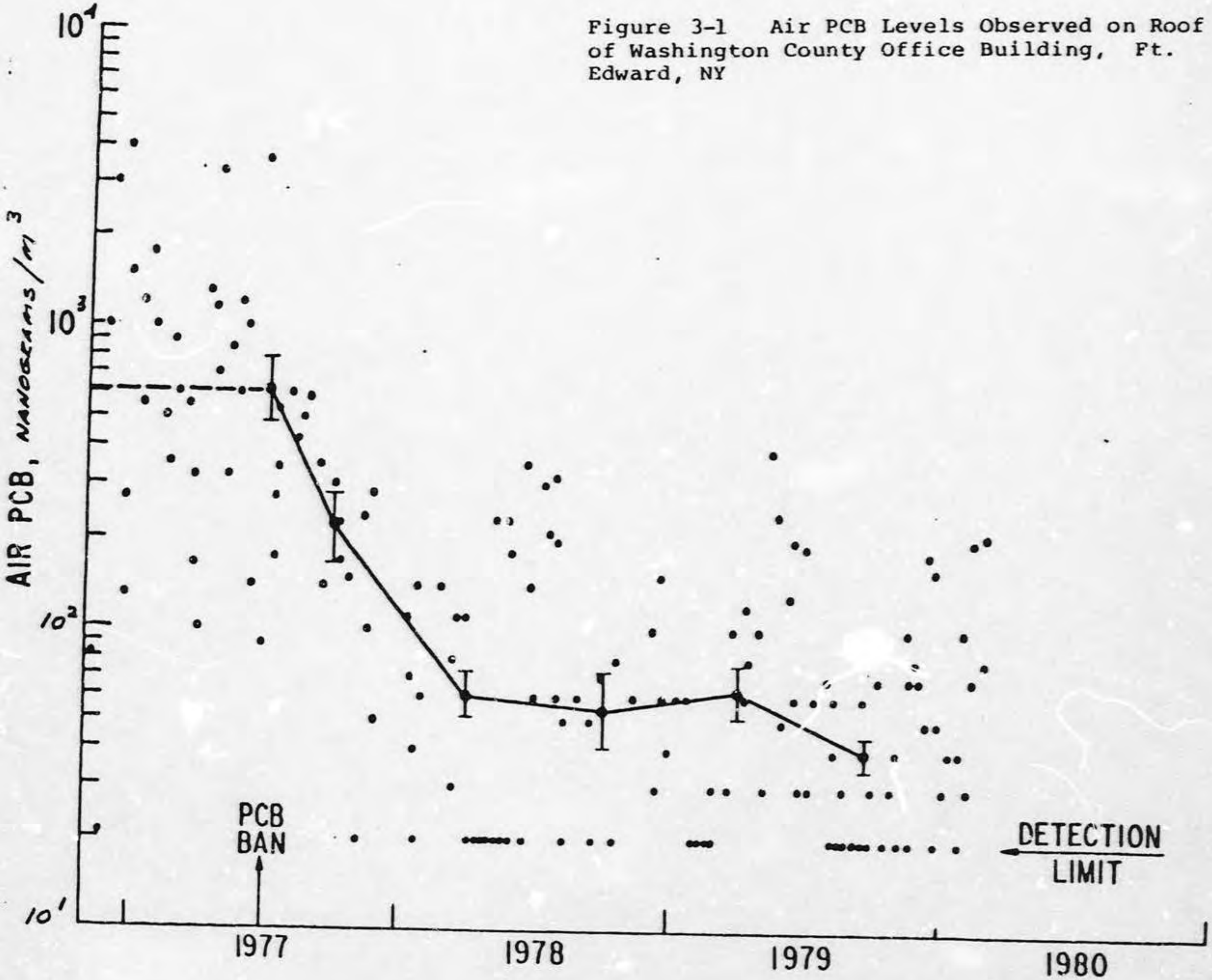


FIGURE 3.1

Figure 3.2

Distribution of Airborne PCB Levels Observed at Hudson Falls and Ft. Edward Plants

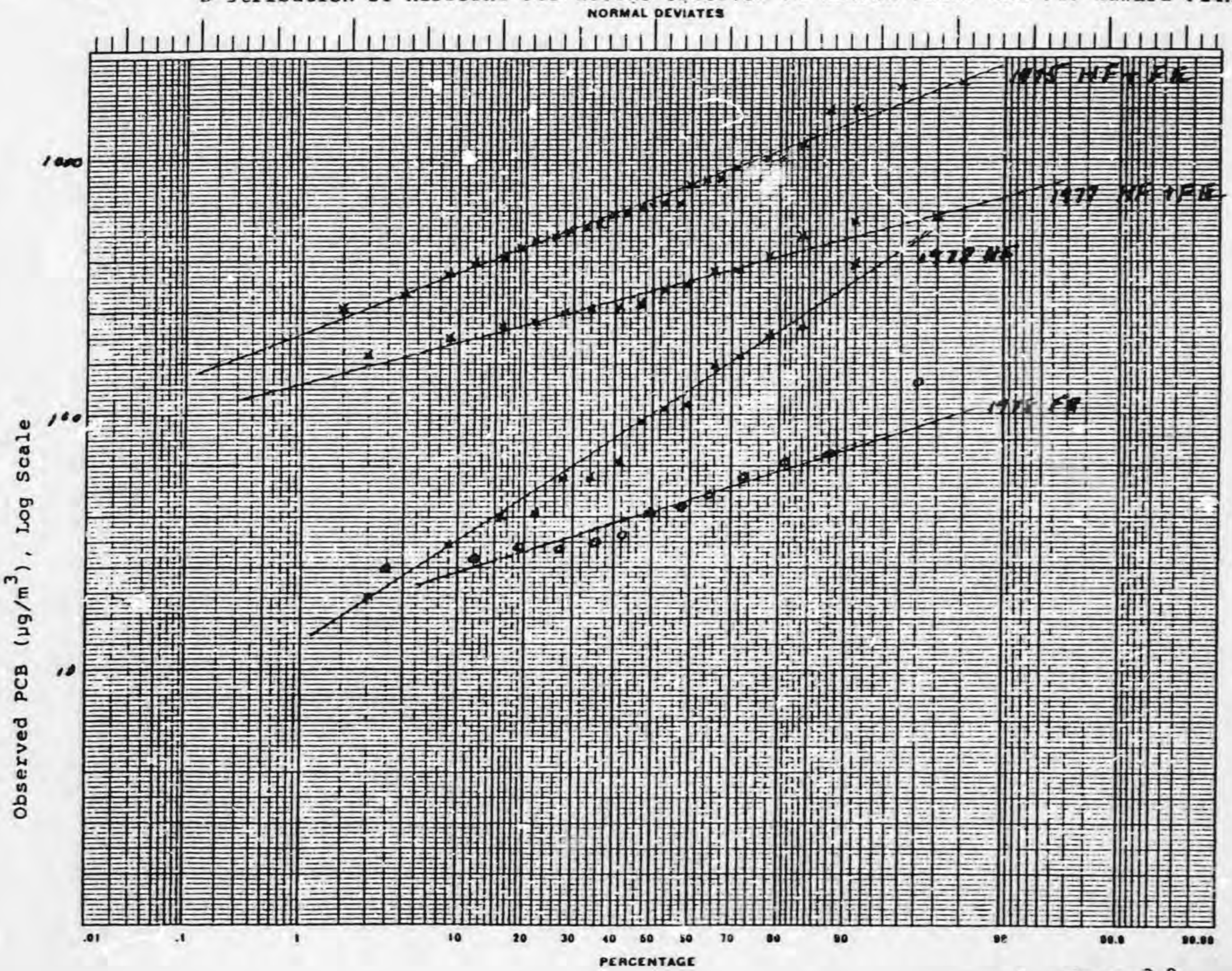


Figure 3.2

TABLE 3-13 GE AIR SAMPLING STUDIES (AREA SAMPLES)

	N	Sampling Time (min)	log $\bar{X}$	log SD	GM $\mu g/m^3$	Arithmetic Mean ± SD $\mu g/m^3$	CV %	$\ddot{X}$
10/23-24/1975 (Toluene)								
Hudson Falls	14	90-400	2.808	0.203	642	704 ± 284	7.24	0.508
Fort Edward	15	60-385	2.881	0.251	761	899 ± 571	8.72	$0.20 < p < 0.35$
Total	29	-	2.846	0.228	701	805 ± 459	8.02	
4/27-28/1977 (Hexane)								
Hudson Falls	8	-	2.508	0.170	322	346 ± 151	6.80	0.388
Fort Edward	8	-	2.474	0.165	298	316 ± 112	6.66	$0.35 < p < 0.40$
Total	16	74-416	2.491	0.163	310	331 ± 129	6.54	
3-7/1978 (Florisil)								
Hudson Falls	16	-	1.991	0.412	98	151 ± 162	20.72	2.35
Fort Edward	13	-	1.638	0.208	43	49 ± 30	12.71	$p < 0.025$
Total	29	-	1.832	0.376	68	105 ± 131	20.54	
12/1980 (Florisil)								
Hudson Falls	20	-	1.363	0.372	23	31 ± 24	27.28	
	16	-	1.610	0.297	41	50 ± 31	18.47	
	20	-	1.537	0.316	34	44 ± 29	20.58	
(Perchlorn)	20	-	1.909	0.322	81	105 ± 79	16.85	
Fort Edward	18	-	1.494	0.439	31	51 ± 56	29.34	
(Perchlorn)	18	-	1.478	0.525	30	56 ± 63	35.53	

TABLE 3–14 NIOSH SITE AUDIT 4/27-28/1977
(FLORISIL)

	N	Sampling Time (min)	log $\bar{X}$	log SD	GM $\mu g/m^3$	Arithmetic Mean ± SD $\mu g/m^3$	CV %	$\bar{t}$
Personal Samples								
Hudson Falls	19	176-427	2.085	0.262	122	143 ± 87	12.58	2.704
Fort Edward	12	271-452	2.294	0.154	197	209 ± 82	6.74	$0.005 < p < 0.01$
Total	31	-	2.213	0.224	163	184 ± 88	10.13	
Area Samples (Non-Treatment Areas)								
Hudson Falls	8	195-427	1.319	0.392	21	27 ± 16	29.73	
Ford Edward	11	387-442	1.749	0.347	56	70 ± 41	19.84	
Total	19	-	1.568	0.417	37	52 ± 39	26.62	

Building, next door to the Fort Edward plant) are shown in Figures 3-3 and 3.1.

The various data compilations permit evaluation of the effects of some, but not all, of the methodological variations in the sampling procedures.

First, as regards sample collection media, the very limited data (that on 1977 area air levels near soldering operations in Tables 3-3 and 3-7) indicate, but certainly do not prove, that the data obtained using hexane are comparable to that obtained using florisil. Second, as regards analytical methodology, the data obtained using the perchlorination procedure on the 1980 Fort Edward samples were comparable to those using the conventional procedure, whereas that obtained on the Hudson Falls samples were clearly deviant. The perchlorination procedure has been used far less than the direct gas chromatographic method of analysis, and its results must still be considered problematical. Finally, comparison of the April 1977 GE data on PCB air levels in the treat, seal and salvage areas (geometric mean, 310 ug/m^3) with the April 1977 NIOSH data obtained from personal air samplers attached to personnel working in those areas (geometric mean, 165 ug/m^3) suggested that the actual levels of respiratory exposure might be only half those indicated by the area air levels, presumably reflecting the tendency of the workers to move in and out of the zones of highest PCB levels.

The area air sampling data indicated PCB levels in the PCB handling areas to have been in the range 260-2000 ug/m^3 (geometric mean, 701 ug/m^3) in 1975, and to have dropped steadily with time over the 1975-1980 period. The 1975 and 1977 samplings, which were confined to those areas of the

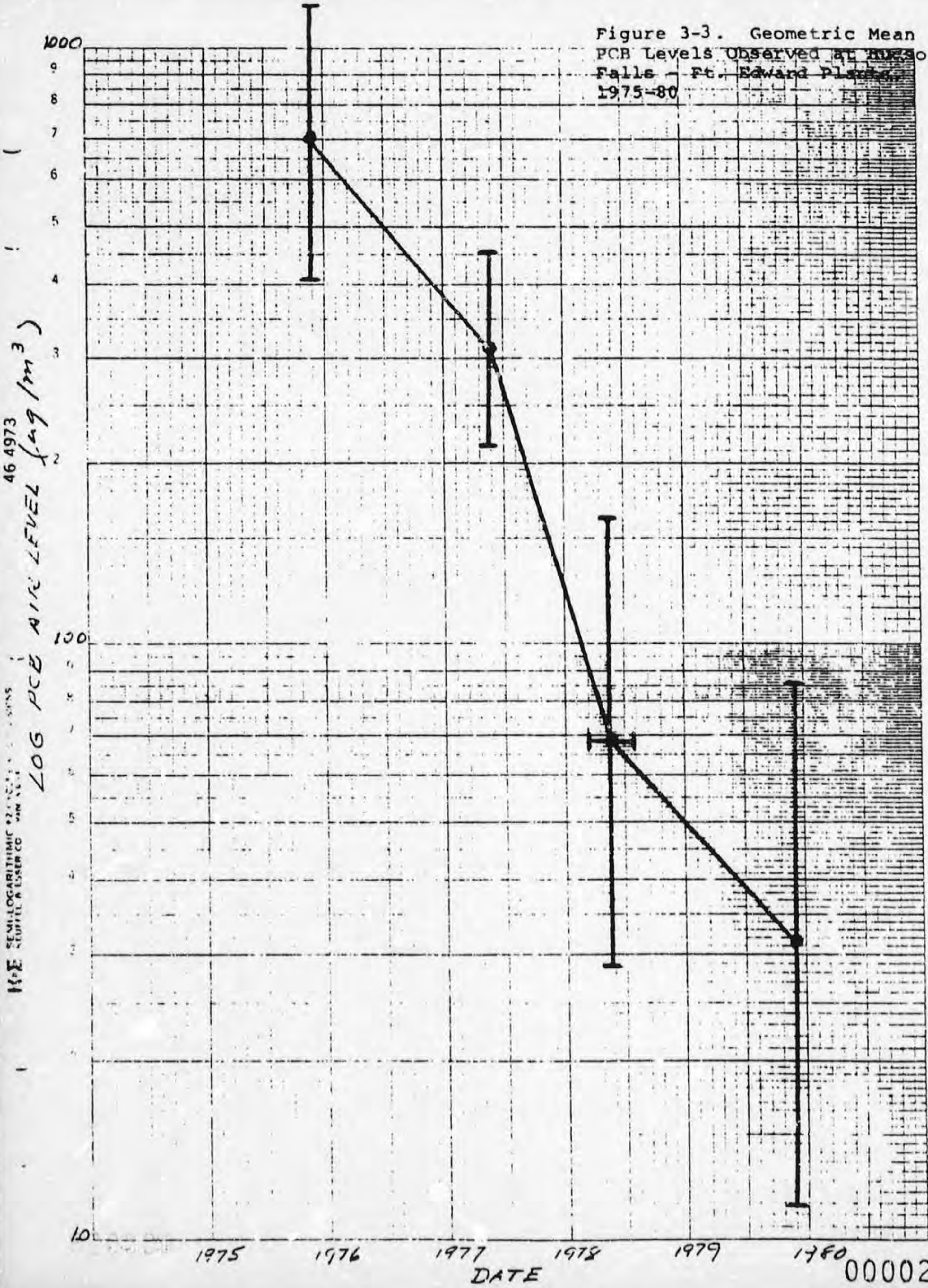


Figure 3-3. Geometric Mean PCB Levels Observed at Hudson Falls – Ft. Edward Plants, 1975-80

plant directly involved in PCB handling, showed no significant differences between the levels at Hudson Falls and those at Fort Edward. The 1978 and 1980 samplings, which covered a wider range of areas in both plants, showed significant differences between the plants both in mean levels and range of levels. Evidently, in the older plant (Hudson Falls) there were more hidden deposits of PCB that eluded the attentions of the 1977-78 clean-up efforts.

The area air sampling data for areas not directly involved in PCB handling operations showed geometric mean levels about 8-fold lower than those for the PCB handling areas in 1977 (37 vs. 310 ug/m^3 for both plants combined), and suggestions of a continuing differential in 1978 and 1980 (Tables 3-8, 3-9, 3-11, 3-12). In 1980, three years after the discontinuance of PCB use, there was still no area inside either plant showing PCB levels significantly under 5 ug/m^3, and the geometric mean for all sampling stations combined was still 31 ug/m^3.

The area air sampling data for stations outside the plant buildings (Tables 3-9, 3-10, 3-11; Fig. 3-1) were more highly scattered, as expected, but did indicate the presence of measurable PCB levels at the County Office Building roof, in the backyard of the industrial hygienist's home, and at some nearby PCB landfill sites. The median levels at the County Office Building dropped from 0.6 ug/m^3 in 1976-77 to 0.04 ug/m^3 in 1979-80.

Thus there is a considerable body of data available concerning PCB air levels in and around the plant during the 1975-80 period. Unfortunately, there is no data whatsoever regarding such levels during the preceding 30 years. One can speculate that the levels inside the plants may have been higher in the late 1950's and early 1960's before the ventilation system was upgraded, or conversely that they may have been lower because massive saturation of the entire plant structure with trichlorobiphenyls had not yet developed. One can also speculate that they should have been much lower in the late 1940's and early 1950's because of the much lower vapor pressure of the pentachlorobiphenyls and the lack of previously accumulated PCB in the plant. However, there are no recorded measurements either to confirm or to deny such speculations. Accordingly, in all endeavors to correlate PCB body burdens with exposure levels, we will be required to make the assumption that PCB air levels measured in 1975 were indeed representative of those present during the entire period of Aroclor 1242 or 1016 use.

As pointed out previously, however, this historical uncertainty need not extend to the question of the composition of the PCB mixture to which plant personnel were exposed in the past. A capacitor is a hermetically sealed device that preserves its contained fluid in the dark, at moderate temperatures, and in the presence of stabilizers. By analysis of old datable capacitors, it should be possible to identify the levels of PCDFs or other toxic contaminants that may have been present at the time of manufacture.

4. Description of Employee Population

The General Electric plants at Hudson Falls and Fort Edward, New York are located near the junction of Washington, Saratoga and Washington Counties, and draw their work force predominantly from those three counties, along with a few people from eastern Vermont. The employee population is estimated to have varied between a low of 1500 and a high of 2000 depending on the business cycle. Hourly production employment is estimated to have varied from 1200 to 1600 over the same period. Approximately 10% of the plant employees had work involving direct physical contact with PCBs.

Figure 4-1 shows the age and service time distributions of the hourly employees, separated according to sex, as of October 1976. The population was bimodally distributed in both age and service time, with one peak around age 30, or 5-15 years service, and a second near age 50, or 20-30 years service. The service times ranged out to 35 years. Seniority and service dates generally agreed within one year, indicating few important breaks in service continuity. Female employees constituted 42.5% of the entire plant population, and 62% of that was in the 55-59 age bracket.

Demographically, the employee population is presumably representative of the industrially-employed population of Saratoga, Warren and Washington Counties. The populations of these counties differ slightly

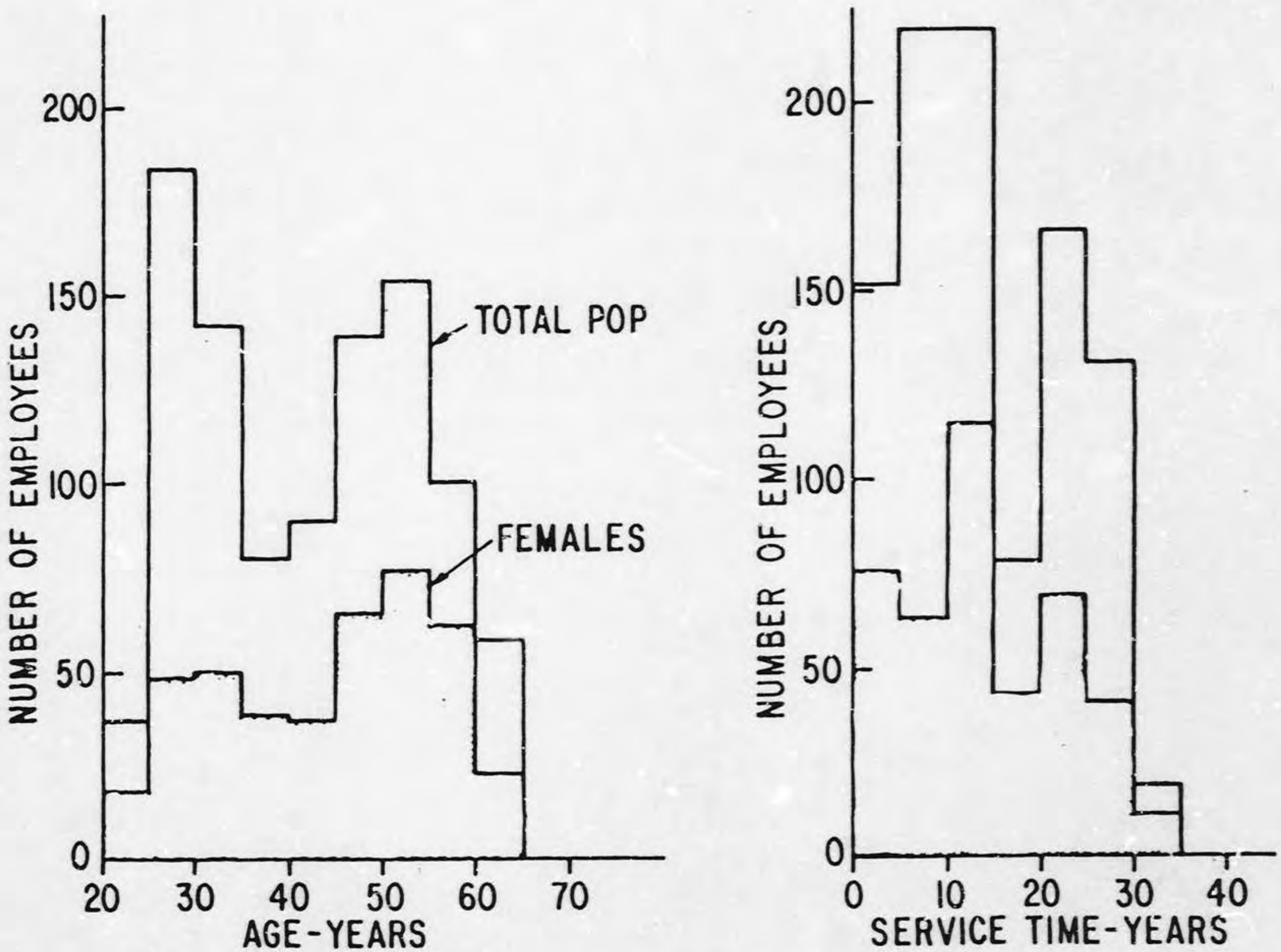


Figure 4-1. Distributions of Hourly Employees of Hudson Falls - Ft. Edward Capacitor Plants by Age and Service Time

from national norms in several respects. The populations are predominantly rural and average 99.1% white, with mostly English or French surnames. The mean fetal death rates in the three counties in 1968 were only 8.8, 6.3, and 3.3 per thousand, respectively, in contrast to 13.6 per thousand for New York State as a whole. Conversely, all these counties shared in the surge in chronic obstructive lung disease that has occurred in upstate New York during the past 20 years.[1] According to the DHEW Atlas of Cancer Mortality, 1950-1969 cancer mortality (all sites) for males was significantly higher than the national average for Warren and Saratoga Counties, with excesses in colon and rectal, lung, and bladder cancers. For females, Warren and Washington Counties had excesses, particularly in ovarian, cervical and rectal carcinomas.

It is not certain to what extent the reported excesses in cancer can be linked to occupational exposure. One small sample of relevant data is provided by Table 4-1, which lists the prior occupational exposures of the 194 individuals selected for clinical examination because of high exposure to PCB (next Section). It is evident from this Table that occupational exposures to a variety of suspect carcinogens were occurring in the 3-county area, but it is not known whether such exposures were in excess of national norms.

Employee Records

The ultimate data bases from which more detailed information about the employee population of the plants must be drawn consist

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[1] Rubin, B.B. Mortality from lung cancer, emphysema, and bronchitis for counties in New York State excluding New York City, 1960-1. New York State Department of Health Monograph No. 16, Albany, N.Y. October 1980.

Table 4-1. Reemployment Occupational Exposures of 194 Hudson Falls - Ft. Edward Capacitor Workers Who Subsequently Had Heavy Exposure to PCB.

Chromate dust and paint pigment	12
Other chemicals and pesticides (farmers, gas station attendents, laboratory personnel, etc.)	22
Lint (shirt, carpet and other factories)	10
Mining, cement, and stone	10
Asbestos (pipefitters, plumbers, electricians, construction)	23
Heavy metals and foundry	10
Military Service - Possible multiple exposures	35
Paper mills	8

of four types of employee personnel and medical records, which are currently being collated and microfilmed for analysis. These records, available for both current and former employees, are the following:

1. Employment application, which provides name, address, social security number, birth date, sex, prior employment history, education, etc.
2. The front page of the personnel record, which lists all jobs held during employment by code, title and dates, absences of over two weeks due to illness, lack of work, leave of absence, etc. in chronological order.
3. Information selected from medical records including physical exams, health insurance data, non-routine visits to the Medical Department and periodic medical evaluations.
4. Physicians Statement. Since 1970, it has been necessary for insurance purposes to submit a physician's report on any employee returning to work after an absence due to illness of two weeks or more. This report indicates the diagnosis, any surgical procedure performed, the period of disability and whether the disability was considered work-related. Prior to 1970, less elaborate reporting was required; however, examinations were conducted on returning employees by the plant physicians and the results, along with the insurance forms, were included in the medical record, so that the information needed to construct morbidity profiles does exist.

One of the desired outcomes of the ongoing studies of PCB blood levels in population sub-groups (described below) and their correlation with job codes is the development of criteria for classifying individuals into exposure categories on the basis of the information contained in their personnel records. Such determinations of exposure category would then be used in the epidemiological analyses of mortality and pregnancy outcome data currently being planned by the New York State Department of Health.

5. Description of Study Populations

As noted at the beginning, this study was initiated as an occupational medical investigation; that is, a deliberate search for clinical abnormalities in the small number of most heavily exposed employees, rather than as an epidemiological investigation of statistical anomalies in a large group of mostly lightly exposed individuals. The procedures used for selecting the study group and subgroups used in this study, and the characteristics of the group selected, will be described in turn.

Selection and Classification Procedures

The initial clinical study group (Group 1) was selected by one of us (M.R.R.), who, as plant nurse and hygienist, had considerable personal knowledge of the plant operations and plant personnel. The criterion for selection was direct (physical contact) occupational exposure to PCB at the time (early 1976), and it was the intent of the selection to have the study group include all employees having current direct exposure. The group selected consisted of 152 males and 42 females, for a total of 194 persons.

This selection procedure differed considerably from that employed at the same plants later in 1976 by a team of investigators from the Mt. Sinai School of Medicine who have already published some preliminary accounts of their findings (by Alvares, Fishbein, Selikoff, et al.). The Mt. Sinai group issued a call for volunteers through the union, and as a result obtained a group of 326 persons.

The available reports indicate that the Mt. Sinai group consisted predominantly of persons having occupational exposures to PCBs that were only indirect, although still well above background. A total of 34 persons were members of both the Mt. Sinai group and the GE group.

In addition to selecting a study population, an effort was made to classify the population selected according to exposure categories. These categories were as follows:

H (high): Individuals with continuous exposure in a high exposure zone.

M (medium): Individuals with short, intermittent exposures in a high exposure zone, e.g., maintenance men.

L (low): Individuals with continuous exposure at the periphery of a high exposure zone.

Unclassified: (Not in Study Group 1): Individuals without direct occupational exposure to PCBs.

These presumptive classifications, made before any data on serum PCB levels were known, have been made available to State and Federal investigators for interim use in epidemiological appraisals. Current indications are that the serum PCB levels in persons assigned to exposure classifications M and L are actually statistically indistinguishable. In addition, serum PCB levels well above background have been observed in the "unclassified" group (those not having direct occupational contact).

Ages and Service Times of Study Group Population

Figures 5-1 and 5-2 describe the distributions of age and service time respectively in Study Group 1. It also shows that these distributions in the study population are fairly similar to those for the plant as a whole.

Job Descriptions and Estimated Exposures

Table 5-1 lists the job descriptions and estimated PCB exposure levels for the 194 persons included in Study Group 1. It is evident that the group comprises individuals performing 57 different jobs, but that only 64 to 100 of the 194 individuals were in jobs assigned to the highest exposure category.

Some information on prior exposures to agents other than PCBs is also available. Table 4-1 listed the prior occupational exposures for the 194 individuals in the study group.

Other Groups Studied

Certain subgroups of Study Group 1 were selected for additional or modified examinations, and some control groups were also selected. The compositions of these additional groups were as follows:

Group 2 was a subgroup of Group 1 comprising 12 individuals whose serum PCB levels were reported to be above 1000 ppb in 1979. Blood samples were drawn from this group in 1980 in order to provide

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000041

Figure 5-1. Distributions of Ages Among PCB-Exposed Capacitor Workers Selected for Clinical Examination, and Comparison with Distributions for Entire Population of Hudson Falls - Ft. Edward Plants

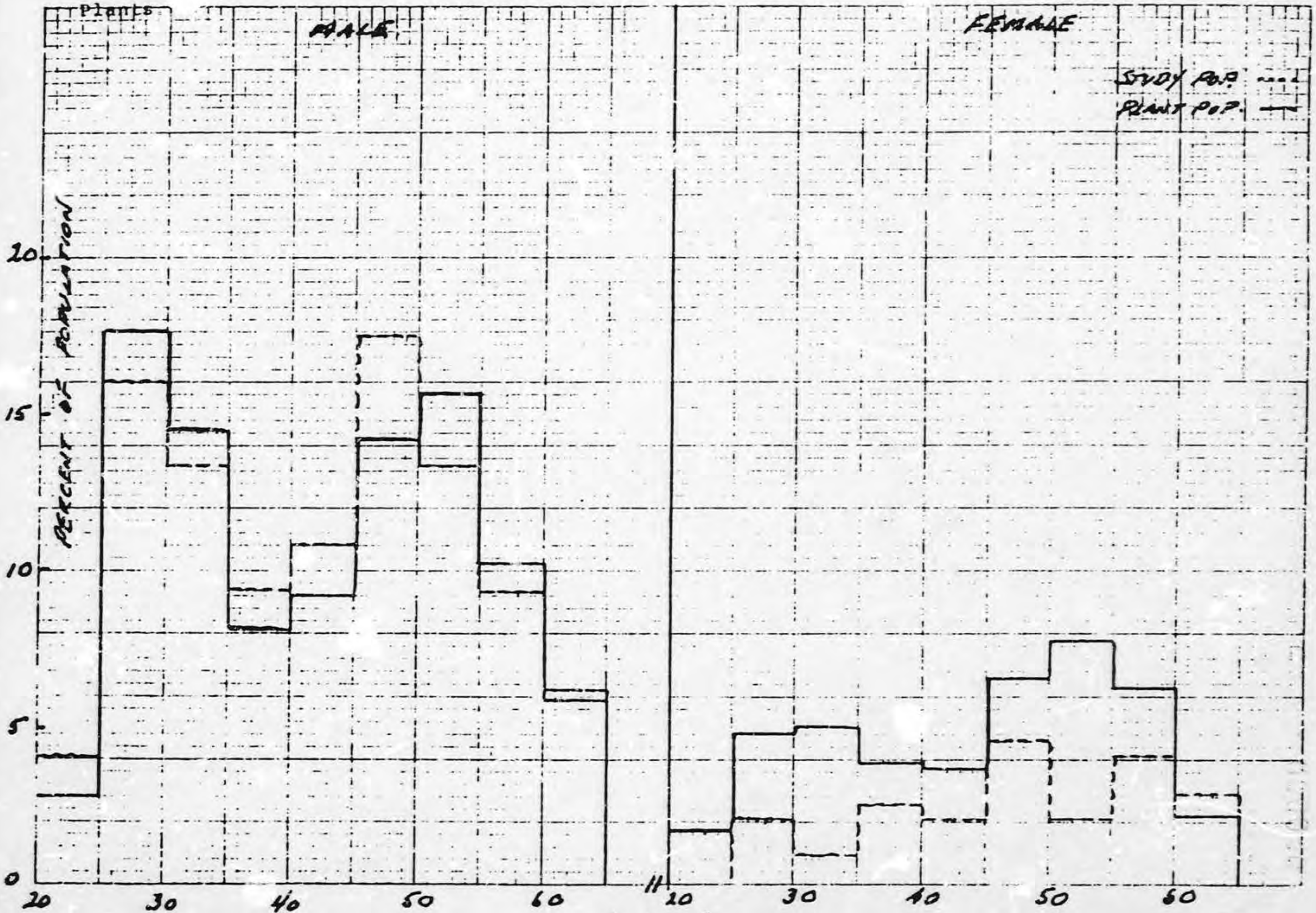

Figure 5-1

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Figure 5-2. Distribution of Service Times Among PCB-Exposed Capacitor Workers Selected for Clinical Examination, and Comparison with Distributions for Entire Population of Hudson Falls - Ft. Edward Plants

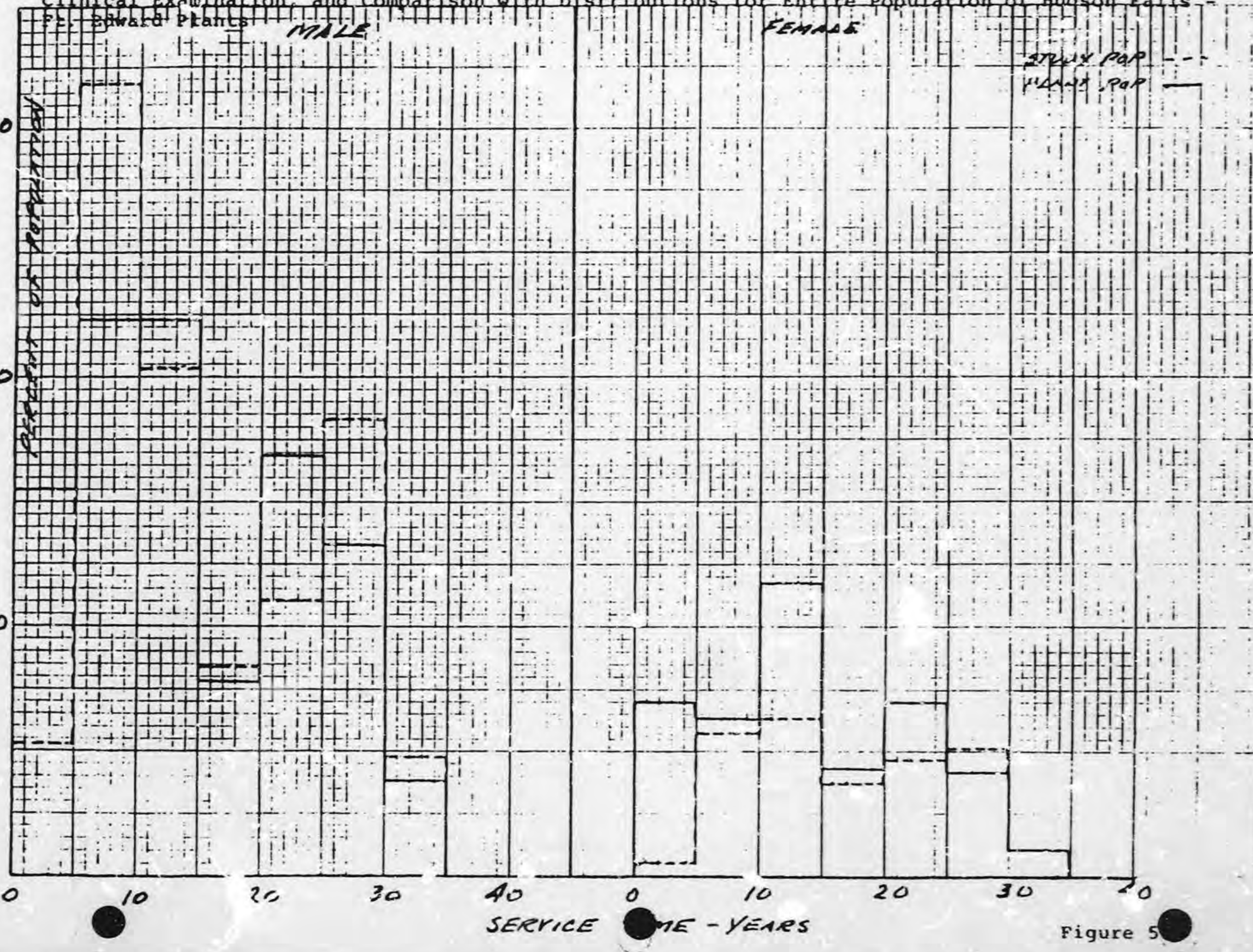

Figure 5

000042

TABLE 5-1. Job Description and Estimated Exposure Levels of PCB-Exposed Capacitor Workers Selected for Clinical Investigation

JOB CODE	TITLE	EXPOSURE LEVEL	NUMBER IN STUDY
0000	Laboratory	L to M	2
7600	Treat Room Operator	H	7
1601	Apprentice PEC	H	8
1213	Plant Engineering Craftsman	M to H	30
6200	Pack & Label/Final Operations Small Industrial Capacitor	L	12
0500	Q.C. Operator	L	2
0000	Manufacturing Analyst	L	2
1214	Plant Engineering Craftsman	L	11
1711	Test Q.C.	H	2
7601	EMF Operator	H	3
0106	Group Leader	L	5
7625	Treat Shift Leader	H	4
0200	Inspector-Incoming Materials	L	1
1317	Moveman	L	18
5514	Seal & Inspect Fillholes	H	7
5750A	Weld Atomic	L	1
0413	Material Follower	H	1
0220	Q.C. Inspector	H	1
5751	Repair Power Factor Capacitor - Heavy	H	1
1420	Repair Power Factor Capacitor	H	7
0000	Power Manufacturing Engineer	H	1
0000	Maintenance Foreman	L	3
1421	Repair - Capacitor Transporting Equipment	H	1
1215	Plant Engineering Craftsman	H	3
1701	Shock & Vibration Test	L	1
0000	Treat Foreman	L to M	2

Table 5-1

TABLE 5-1 (continued). Job Descriptions and Estimated Exposure Levels of PCB-Exposed Capacitor Workers Selected for Clinical Investigation

JOB CODE	TITLE	EXPOSURE LEVEL	NUMBER IN STUDY
1401	Salvage - Small Industrial Capacitor	M to H	6
0000	Environmental Quality Engineer	L	1
1707	Test Miscellaneous Repetitive	L	7
1403	Salvage Operator - Power Capacitor	H	2
7607	Refinery Operator	H	4
0000	Manufacturing Engineer	H	3
5702	Load and Unload Welding Machine - Automatic	H	1
0932	Material Handler	L	1
7605	Treat Room Helper - Power Factor Capacitor	H	2
0000	Treat & Test Manager	L	1
0000	Process Control Engineer	L	2
1703	Electrical Tester	L	2
1708	Manual Tester	L	2
0000	Technician	H	2
0000	Safety Specialist	L	1
0619	Tool Crib Keeper - Class A	L	1
3214	Machine Operator - Small Industrial Crimp	H	2
1710	Test Special	H	2
0000	Process Control Specialist	L	2
0000	Quality Control	L	1
0000	Methods/Time Standards	L	1
0000	Production Control	L	1
0000	Facilities Analyst	L	1
0000	Analytical Chemist	L	1
0000	Quality Control Engineer	L	1
0000	Shipping Foreman	L	1

Table 5-1

TABLE 5-1 (continued). Job Descriptions and Estimated Exposure Levels of PCB-Exposed Capacitor Workers Selected for Clinical Investigation

JOB CODE	TITLE	EXPOSURE LEVEL	NUMBER IN STUDY
0000	Engineer	L	1
0000	Manufacturing Specialist	L	2
1280	Development Specialist	L	1
0000	Maintenance Supervisor	L	1
0000	Manager - Components	L	1
	TOTAL		194

the individual and pooled samples used to evaluate the precision of the serum PCB analysis as described in Section 7. This group is thus our only source of information about 1979-80 changes in serum PCB levels.

Group 3 consisted of 18 office workers at the GE Corporate Headquarters in Fairfield, Connecticut, none of whom had ever had any known occupational exposure to PCB's. Blood samples were drawn from this group in order to assess serum PCB background levels in 1976 and 1979.

Group 4 consisted of 18 subjects drawn from the Hudson Falls-Ft. Edward salaried administrative staff. These were individuals who had had long service at the plants (average, 23.6 years), but no known direct occupational exposure to PCB's. This group is believed to be comparable in exposure history to most of the older employees in the volunteer group examined by the Mt. Sinai investigators.

Group 5 consisted of 16 capacitor workers currently working in the impregnation operation, but employed since the 1977 discontinuance of PCB use. These individuals were young and averaged only 2 years' service time.

Group 6 consists of 20 individuals who were originally members of Study Group 1, but who have subsequently retired or left the Company. Some missed the 1979 follow-up of the initial 1976 examination. An effort is now being made to track down these Group 1 alumni and persuade them to undergo continuing examinations in order to assess PCB clearance rates and development of PCB relatable health problems (if any) in the older age groups. Formal arrangements are also being made to include a PCB follow-up request as a part of the pre-retirement exit interview.

6. Clinical Examination Procedure

Following the 1976 selection of 194 employees for study, they were invited to the Medical Dispensary for workup. A medical history was taken and a physical examination performed by the attending physician (J.F.). Blood was drawn for PCB levels and conventional chemistries, and pulmonary function was assessed by spirometry. ECGs were obtained and read by one of us (J.F.). Chest X-rays were obtained and read by a local radiologist. Each employee received a letter outlining any abnormal findings. In appropriate cases, the findings were discussed with the employee and the data forwarded to his or her physician. PCB levels were not divulged or discussed with employees.

The study group was brought back for reexamination during November 1979. The reexamination consisted of an updating of the medical history, a more exact definition of smoking habits and further data on reproduction. Pulmonary function tests were repeated. Chest X-rays, ECGs and physical examinations were repeated only in selected cases. Blood chemistries and PCB levels were again obtained. The data obtained in 1976 and 1979 has been supplemented by interim examinations and by follow-up examinations since November 1979.

About half of the Mt. Sinai group re-volunteered for a repeat examination in December 1979. No findings from this second Mt. Sinai examination have yet become available.

Blood Chemistries

Fasting blood samples were drawn at the time of medical examination for blood chemistries ahd hematology, and a urinalysis performed. The analyses were conducted under contract by Metpath, Teterboro, New Jersey. Table 6-1 lists the blood, hematological and other variables measured in this study. Between 1976 and 1979, total lipids were dropped from the routine Chemscreen and magnesium added so that 1976-1979 comparisons are not possible for these variables.

In 1979, Metpath introduced a computer program that provides a statistical summary of analyses performed for individual institutions. A part of the output consists of tables of normal ranges adjusted for age and sex. We have made use of these standards in the evaluation of our data. All data in the Metpath analyses are treated as normal distributions, although there is substantial evidence that many of the variables of interest in this study, primarily those related to liver function and blood lipids, are actually lognormally distributed. Where appropriate, we have also evaluated the data using the log-normal assumption.

TABLE 6-1. Clinical Parameters Evaluated During Examinations of PCB-Exposed Capacitor Workers at Hudson Falls - Ft. Edward Plants

Population and Exposure (16)

- Sex
- Age (years)
- Service (years)
- Job Code
- Job Status (active, inactive)
- Plant (HF or FE)
- Exempt/Non-Exempt
- Disease Status

- Serum PCB
- Aroclor 1242 (Lower homologs)
- Aroclor 1254
- Aroclor 1260 (Higher homologs)
- P,P'-DDE
- Exposure Estimate (0-2)
- Air PCB
- Mt. Sinai Participation
- Fast/Non-Fasting (1976)

Metabolism (11)

- Height
- Frame
- Pre-Empl. Wt.
- Body Wt. (76 & 79)
- Max. Ref. Wt.
- Body Wt/Height*
- Body Fat (kgs. or % BW)
- Triglycerides
- Cholesterol
- Blood Sugar
- Uric Acid

Cardiovascular Function (3)

- ECG
- Blood Pressure
  - Systolic
  - Diastolic

Liver Function (12)

- Total Bilirubin
- Direct Bilirubin
- SGOT
- SGPT
- GGTP
- Alkaline Phosph.
- LDH
- Total Protein
- Albumin
- Globulin
- A/G Ratio
- Amylase

Renal Function (17)

- Bun
- Creatinine
- Bun/Creat. Ratio
- Na+
- K+
- Cl-
- Ca++
- Ph-

Urinalysis

- Appearance
- pH

- Sp. Gr.
- Acetone
- Albumin
- Glucose
- RBC
- WBC
- Casts

Hematology (13)

- Iron
- RBC
- HGB
- HCT
- MCV
- MCH
- MCHC
- WBC
- Differential
  - Polys
  - Lymphs
  - Monos
  - Eosins
  - Baso.

Pulmonary Function (4)

- FVC
- FEV_1
- FEV_1/FVC
- Chest x-ray

History (5)

- Smoking
- Alcohol use*
- Drug use*
- Diagnosis
- Surgery

Symptomatology (6)

- Dermatological
- Neurological
- Cardiovascular
- Respiratory
- Gastrointestinal
- Musculoskeletal

...netic...

...ary function was evaluated in 1976 using a Vanguard*

...ith an analog output. Measurements were made in the ... with a disp... filter sensor. Computations of ... and the FEV_1-FVC ratio were performed manually ... from tracings and slide rule. Measurements were judged acceptable when there was agreement within 10 percent in two out of three repetitions.

The 1979 measurements were made with a Vanguard* DS 502 spirometer with a preprogrammed computer printout that utilized the Morris standards[2]. In interpreting the data, we have calculated the data following Knudson[3] and broadened the normal range to >70 percent for both vital capacity and the FEV_1/FVC as recommended by the American Thoracic Society. Such standards are important in evaluating the prevalence of restrictive disease found by Warshaw et al.[4] in this population.

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* Life Support Engineering Corp., Woburn, MA

2. Morris, J.F., Koski, A., and L.C. Johnson. Spirometric Standards for Healthy, Non-smoking Adults. Am. Rev. Resp. Dis. 103: 57-67, 1971.

3. Knudson, R.J., Slatin, R.C., Lebowitz, M.D., and B. Burrowo. The Maximum Expiratory Flow Volume Curve: Normal Standards, Variability, and Effects of Age. Am. Rev. Resp. Dis. 113: 587, 1976.

4. Warshaw, R., Fischbein, A., Thornton, J., Miller, A., and I.J. Selikoff. Decrease in Vital Capacity in PCB-Exposed Workers in a Capacitor Manufacturing Facility. Ann. N.Y. Acad. Sci. 320: 277-283, 1979.

7. Serum PCB Measurements

The analysis for PCB's in environmental, biological, or clinical specimens at ppb o ppm levels has been a commercially available service for some half a dozen years, and is now offered by at least a dozen commercial laboratories in this country, including the one engaged for this project. Despite this, serum PCB determinations continue to present far greater levels of imprecision, inaccuracy, and ambiguity in the nature of the parameter reported by the analyst than are encountered in any of the conventional blood chemical measurements commonly used in clinical medicine. Accordingly, we have given continuing attention to the problem of defining the reliability and meaning of the data being supplied to us by our analyst. In this Section we shall describe the sampling and analytical procedures used for the determination of serum PCB levels and present the available data on the accuracy, precision, and significance of the measurements.

Sampling Procedure

Ten cc blood samples were drawn, allowed to clot, centrifuged, and the serum decanted, labelled, and frozen. Groups of samples were shipped in polyethylene containers to WARF Industries, Inc., Madison, Wisconsin (now Raltech) fc nalysis. Serum PCB analysis was begun only in the middle of the study; as a consequence, subjects had to be recalled at odd hours so that the bulk of 1976 PCB samples were taken non-fasting. The balance of the subjects (34) were drawn in the fasting state with the other blood chemistries. In the 1979 study all samples were drawn in the fasting state. In 1976 analyses were reported as Aroclor 1254, Aroclor 1242, and p,p'- DDE using appropriate standards. In 1979, data were also reported as Aroclor 126 .

Analytical Procedures Used

A 1981 description of the analytical procedures used by Raltech, along with some representative chromatograms, is presented in Table 7-1 in uncondensed form, except for the omission of the extraneous chromatograms relating to the DEHP (di-2-ethylhexyl phthalate), TCB (trichlorobenzene), and DCB (decachlorobiphenyl). (The DEHP and TCB levels in the capacitor worker population are not yet known, and Raltech's attempts to determine total serum PCBs by the perchlorination procedure, which would produce DCB for quantitation, have thus far proven unsatisfactory.) We were informed that the PCB analytical procedures used in 1980 on the 1979 serum samples were substantially identical to those in the 1981 descriptions; but did note from the chromatograms that somewhat different peaks had been used in making the quantitations.

The procedure used in 1976, when WARF was just beginning to do such analyses on a commercial basis, differed in several respects, notably in the use of a "petroleum ether-freeze-by-dry-ice" (PE) rather than a "methanol-hexane" (MH) extraction procedure, in the dimensions of the column used (8 ft x 2 mm i.d., rather than 6 ft x 4 mm i.d.), in the source used in the electron capture detector (^{98}St rather than ^{63}Ni), and in the electronic circuitry.

Tests of Accuracy of Procedures Used

The possible significance of these variations between the analytical procedures used in 1976 and 1979 became of great interest when

TABLE 7-1. Description of Procedure for Serum PCB Analysis Supplied by Raltech in 1981

Methanol-Hexane Method (1979)

1. Weigh 5 g of serum into a culture tube.

2. Add 2 mL of methanol* and mix on a Vortex for 1 minute.

3. Add 5 mL of hexane:ethyl ether (1:1) and place on a horizontal shaker for 10 to 15 minutes. If emulsions form, centrifuge and/or place in a sonic bath.

4. Decant hexane layer into a culture tube and repeat extraction two more times with 5 mL of hexane:ethyl ether (1:1).

5. Concentrate under a gentle stream of nitrogen to about 0.5 mL or less.

6. Transfer the extract to a micro-Florisil column. This column is a 2 ft by 6 mm id glass column containing 2.2 g of Florisil (60/100 mesh Florisil, PR grade, from the Floridin Co. [Pittsburgh, PA], heated in a 140°C oven for 16-24 hours).

7a. Elute PCB and DDE with 10 mL 1% methanol in petroleum ether. Concentrate under a gentle stream of nitrogen to about 0.5 mL. Bring volume to 2 mL.

7b. Elute TCB and DEHP successively in the following manner:

First, elute TCBs with 4 mL of 1% methanol in petroleum ether.
Second, elute DEHP with 14 mL of 20% ethyl ether in petroleum ether.

Concentrate on a water bath using micro-Snyder columns and 25-mL concentrator tubes (Kuderna-Danish) to approximately 0.5 mL. Bring volume to 2 mL in calibrated tubes.

8a. Inject blanks, controls, and samples for PCB and DDE on a Hewlett Packard gas chromatograph under the following instrument operating conditions.

Model 5710A GC equipped with electron capture detector
Column: 6 ft x 4 mm id, 1.5% on SP2250/1.95% SP2401 on 100/120 Supelcoport
Temperature
Injector: 250°C
Column: 205°C
Detector: 300°C
Carrier gas: argon:methane (95:5)
Flow rate: 43.5 mL/minute
Recorder: 1 mv, 15 in./hour
Attenuation: 64 (low level)
512 (high level)

* All solvents used were Burdick and Jackson distilled in glass - P.R. grade or equivalent.

Table 7-1 (continued)

8b. Inject blanks, control serum, and samples for TCB on a Hewlett Packard gas chromatograph with the following operating conditions.

Model 5710A equipped with electron capture detector
Column: 6 ft x 4 mm id, 3% OV-1 on 80/100 Gas Chrom Q
Temperature
Injector: 250°C
Column: 125°C
Detector: 300°C
Carrier gas: argon:methane (95:5)
Flow rate: 60.0 mL/minute
Recorder: 1 mv, 15 in./hour
Attenuation: 8

8c. Inject blanks, controls, and samples for DEHP on a Hewlett Packard gas chromatograph operated under the following conditions.

Model 5710A equipped with electron capture detector
Column: 6 ft x 4 mm id 3% OV-1 on 80/100 Gas Chrom Q
Temperature
Injector: 250°C
Column: 240°C
Detector: 300°C
Carrier gas: argon:methane (95:5)
Flow rate: 60.0 mL/minute
Recorder: 1 mv, 15 in./hour
Attenuation: 8

9. Calculations

The baselines for all chromatograms were drawn using a straight edge under all peaks in the chromatogram (Figures 1 to 12).

Aroclor 1242

The concentration of Aroclor 1242 in samples is determined by peak height comparison of sample to standard using three major peaks found at these retention times* in the Aroclor standard: 0.35, 0.70, 0.83.

In the standard, the peak at 0.70 retention time has a small shoulder peak at 0.65. This peak was one of the major peaks in the pooled serum sample chromatograms, therefore the shoulder peaks at 0.65 retention time in the samples was used for quantitation. Figures 2 and 5 depict the standard peaks and corresponding serum sample peaks, respectively. Figure 6 is a chromatogram of a control serum sample which illustrates the peaks used for quantitation.

* All retention times referenced were taken relative to DDE standard with the retention time of DDE = 1.0.

TABLE 7-1 (continued). Description of Procedure for Serum PCB Analysis Supplied by Raltech in 1981

For Aroclor 1242, the equation used for calculation was as follows:

$$\text{Aroclor 1242 (ppb)} = \frac{a \times b \times e}{c \times d}$$

where a = Aroclor in standard peaks (ng)
b = height of sample peaks = (peak height at RT* DDE 0.35 + peak height at RT 0.65 + peak height at RT DDE 0.83)
c = height of standard peak = (peak height at RT DDE 0.35 + peak height at RT DDE 0.70 + peak height at RT DDE 0.83)
d = original sample weight (g)
e = final extract volume (mL)

Aroclor 1254

The peaks used for quantitating Aroclor 1254 were the last four major peaks in the Aroclor standard, at the following retention times: 1.26, 1.42, 1.62, 1.84.

Figure 3 shows standard peaks and Figures 5 and 6 show peaks in pool and control sera.

Calculations are the same as for Aroclor 1242 except:

b = height of sample peaks = (peak height at RT 1.26 + peak height at RT 1.42 + peak height at RT DDE 1.62)
c = height of standard peak = (peak height at RT DDE 1.26 + peak height at RT DDE 1.62 + peak height at RT DDE 1.84)

Aroclor 1260

Three major peaks following the Aroclor 1254 peaks were used to quantitate Aroclor 1260 in the same manner as the previous Aroclors. Peaks measured and used for calculation are shown in the standard in Figure 4 and in pool and control sera in Figures 5 and 6.

Calculations were the same as for the other Aroclors, using the peaks at the following retention times: 1.97, 2.90, 3.77.

DDE

This pesticide was quantitated using peak height comparison of the samples to a standard. The calculation was similar to that for the Aroclors, except that only a single peak was used:

$$\text{DDE (ppb)} = \frac{a \times b \times e}{c \times d}$$

* Retention Time

Table 7-1 (continued)

where a = DDE in standard peaks (ng)
b = height of sample peak
c = height of standard peak
d = weight of original sample (g)
e = final extract volume (mL)

Typical DDE chromatograms are illustrated in Figure 1 (standard) and Figures 5 and 6 (pool and control sera).

DEHP and TCB

DEHP and TCB were quantitated from single peaks. The calculation was identical to the calculation for DDE. A DEHP standard chromatogram is shown in Figure 7 and a serum sample injection is shown in Figure 8. Figures 9 and 10 are representative chromatograms for TCB standard and spiked serum, respectively.

Decachlorobiphenyl

DCB was quantitated from a single peak with a calculation routine identical to that of DDE. Many chromatograms are included in this area of the study, including a DCB standard (Figure 11), an antimony pentachloride perchlorination blank (Figure 12), a perchlorinated control serum sample (Figure 13), and several examples of Aroclor standard perchlorinations.

TABLE 7-1 (continued)

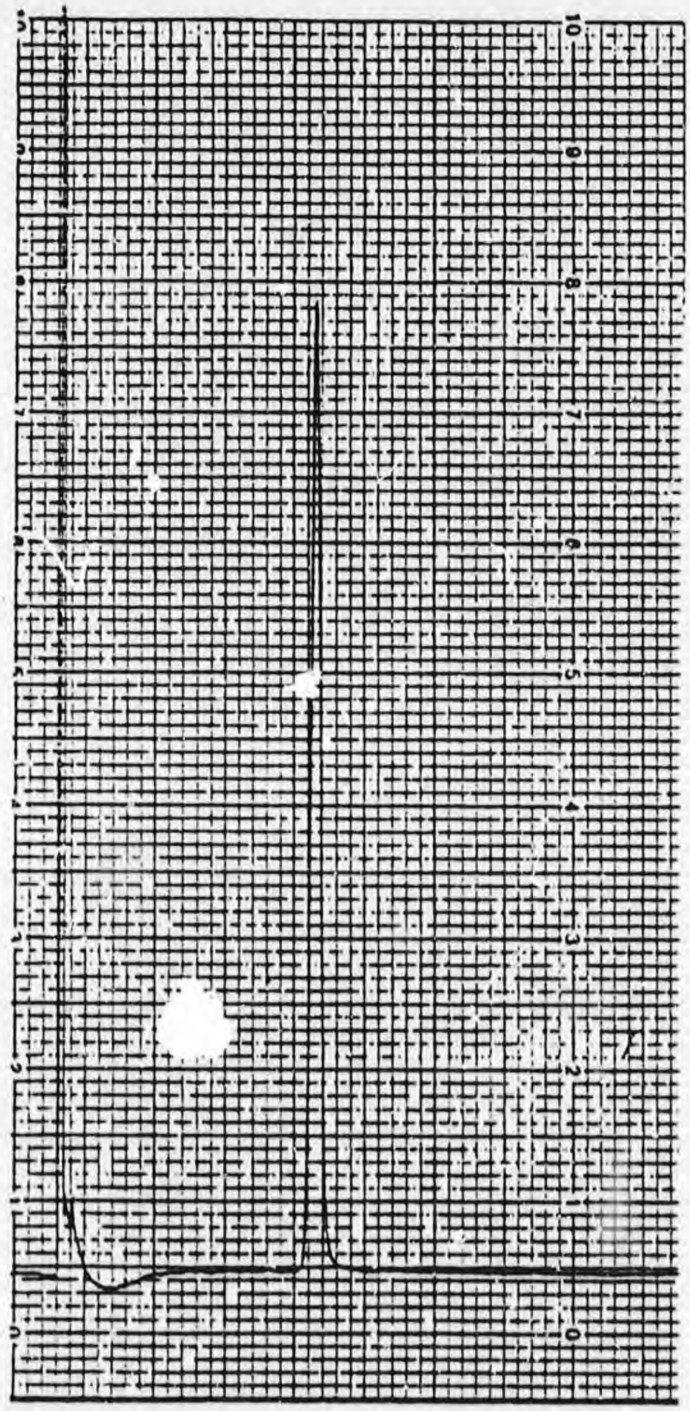


FIG. 1 DDE STANDARD

Table 7-1 (continued)

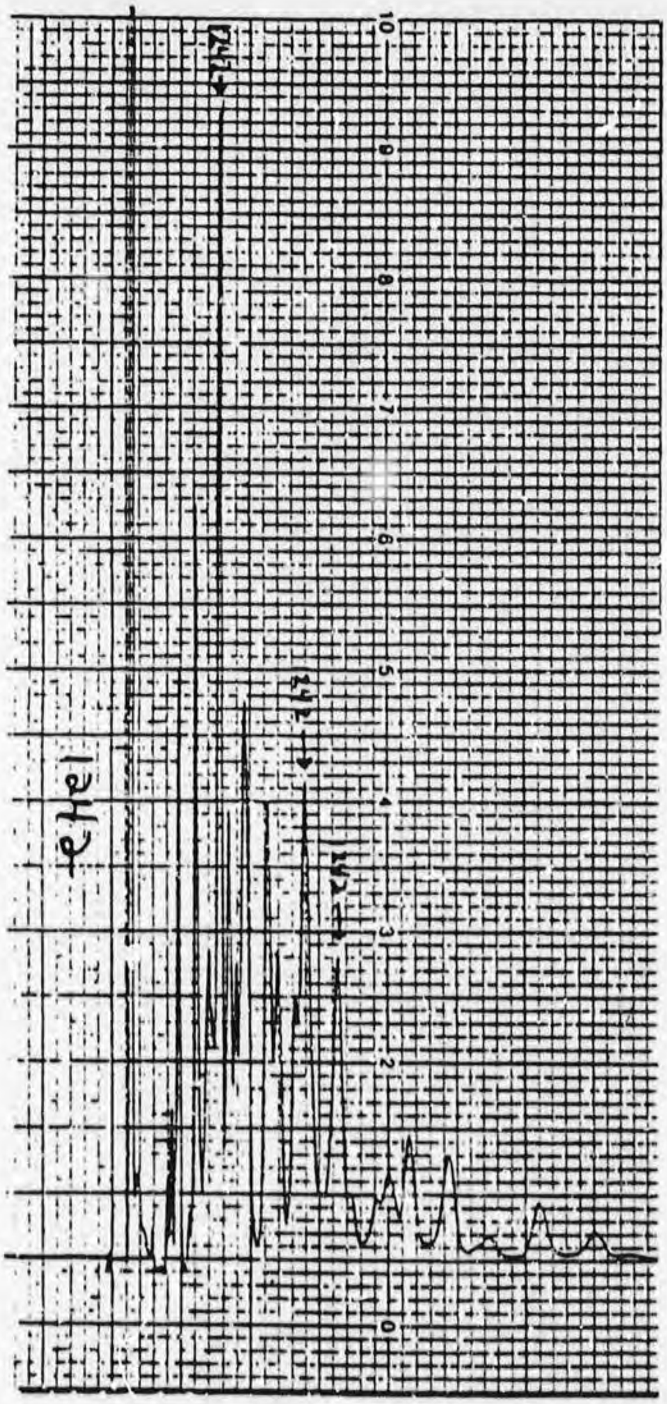


FIG. 2 AROCLOR 1242 STANDARD

TABLE 7-1 (continued)

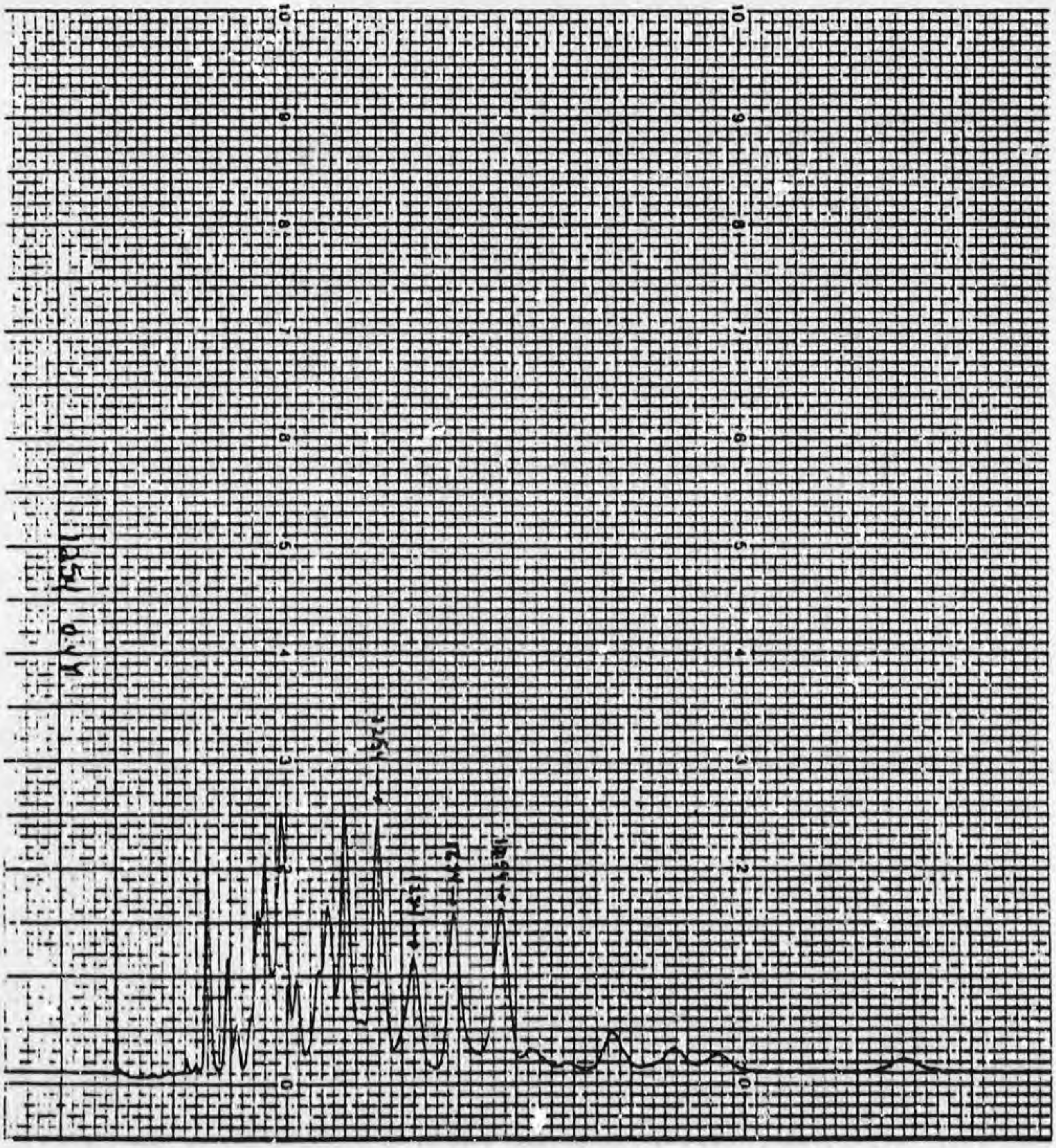


FIG. 3 AROCLOR 1254 STANDARD

Table 7-1 (continued)

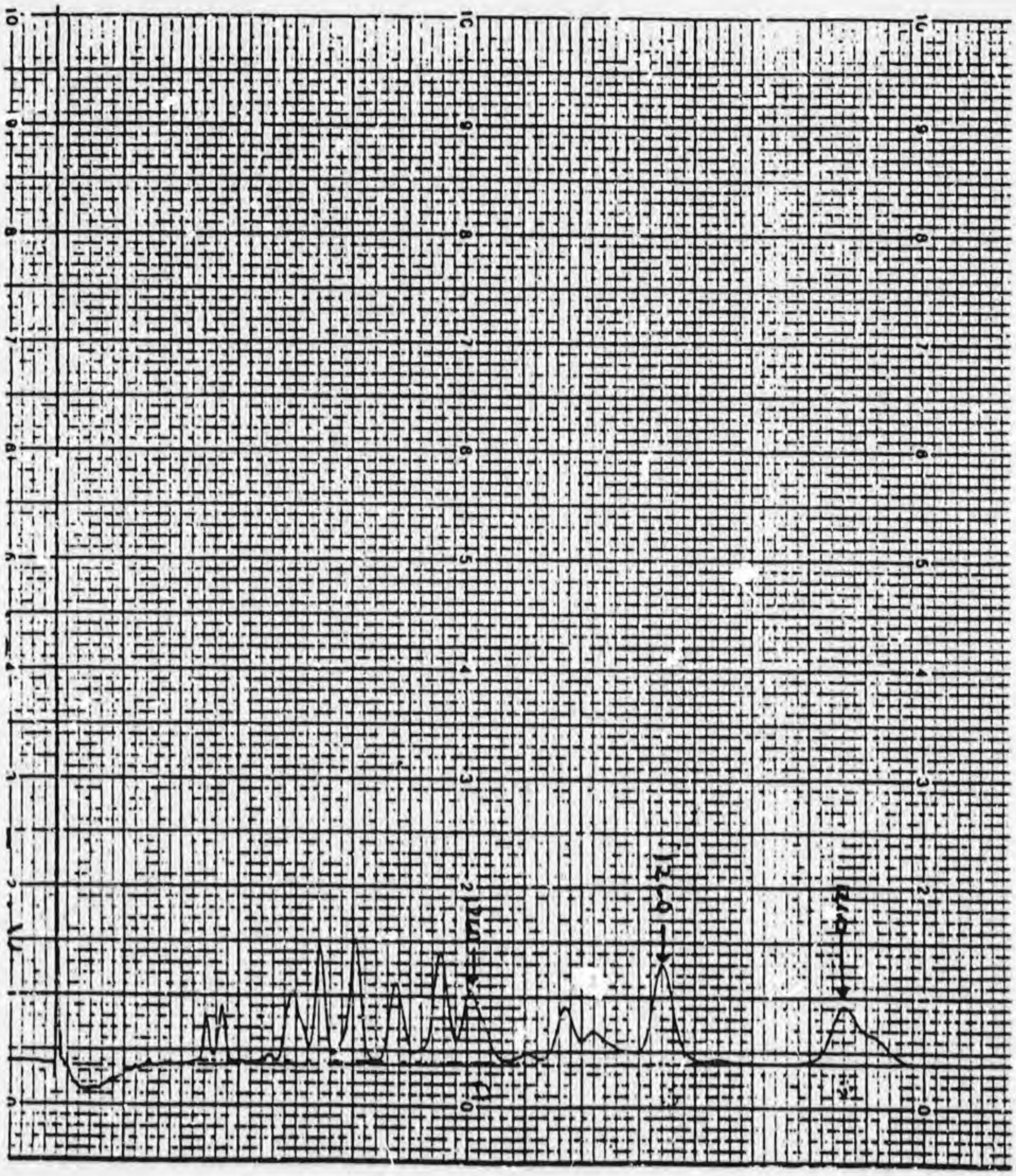


FIG. 4 AROCLOR 1260 STANDARD

TABLE 7-1 (continued)

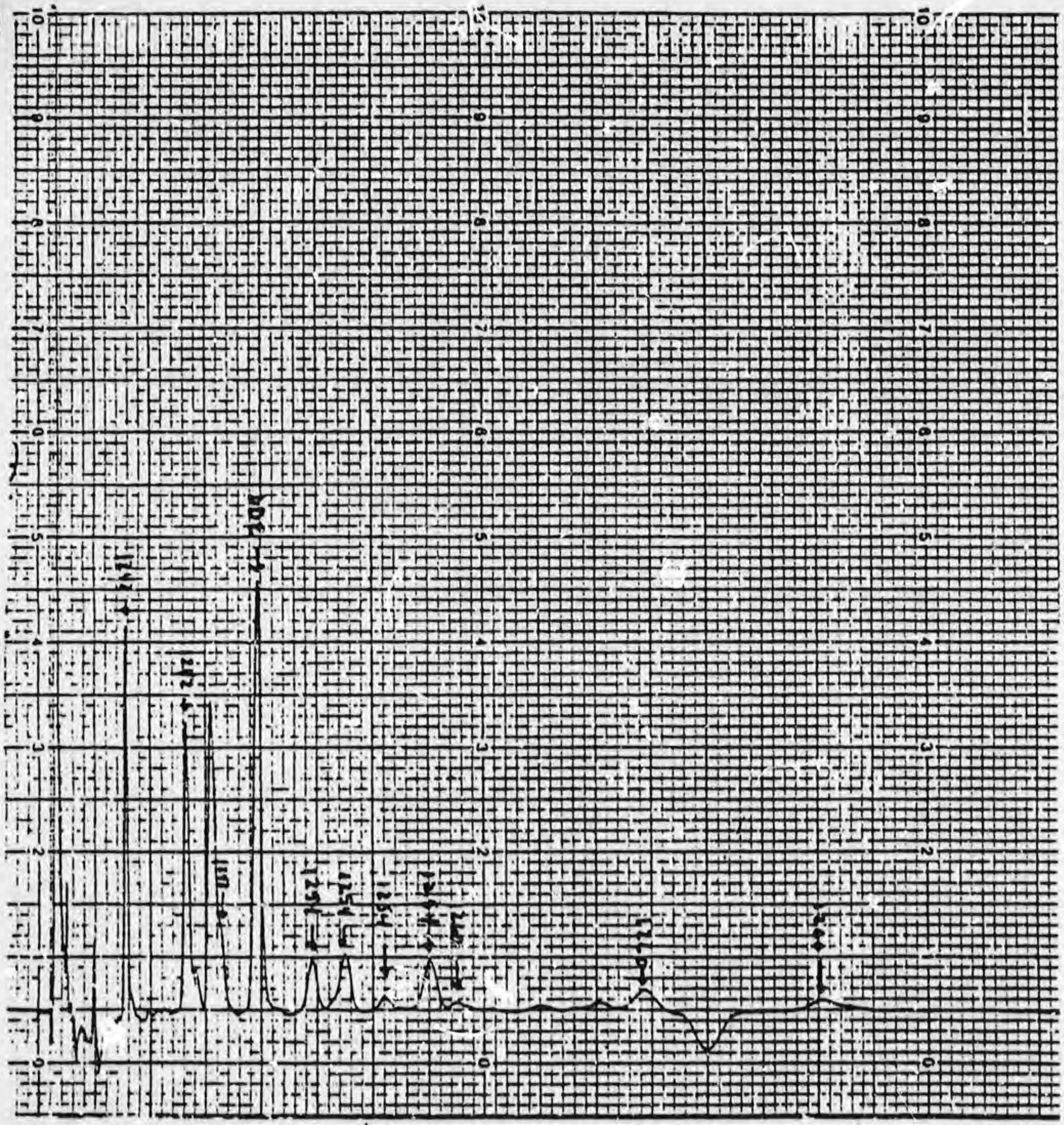


FIG. 5 POOL DILUTION 3A

Table 7-1 (continued)

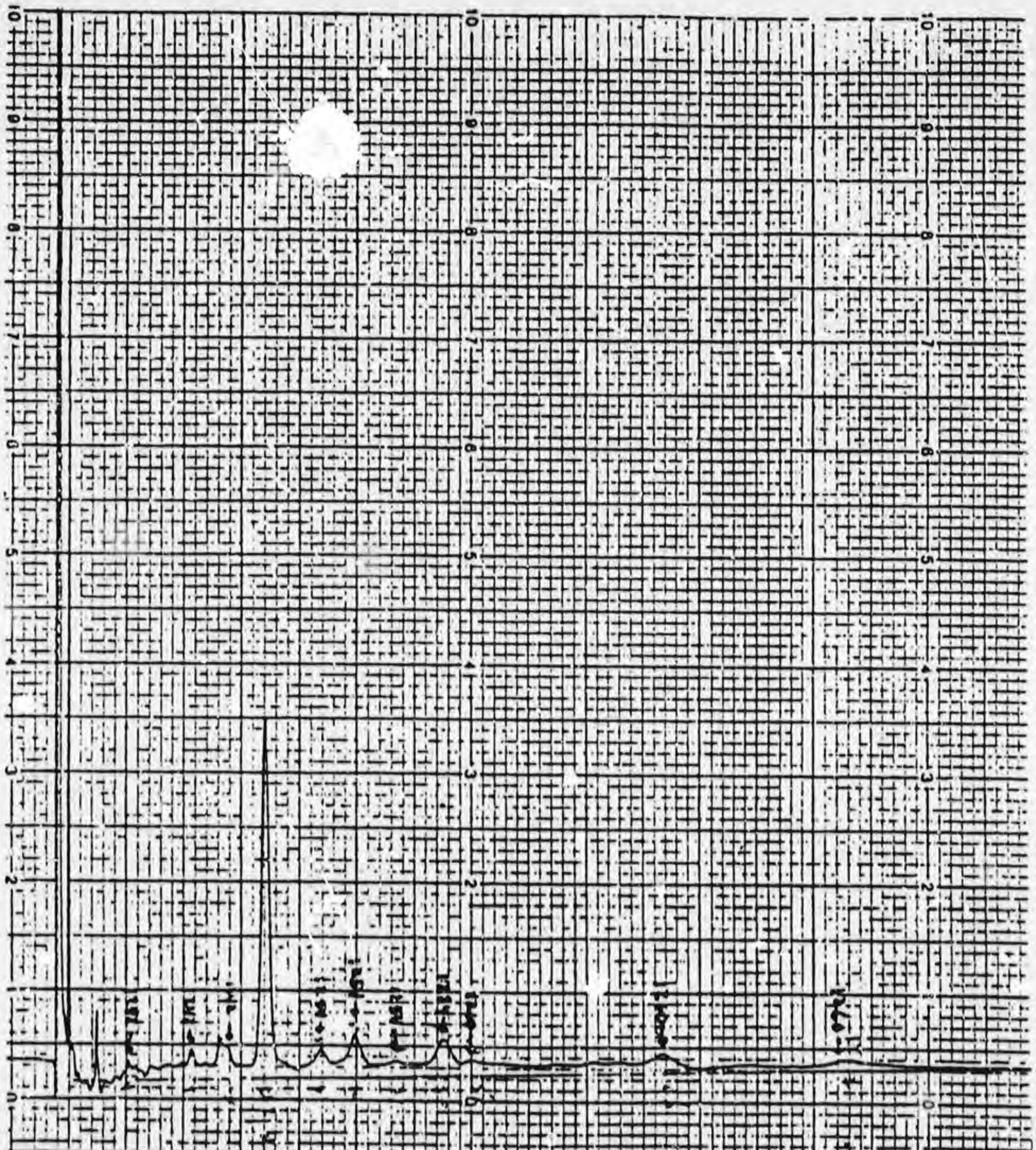


FIGURE 6
REPRESENTATIVE CHROMATOGRAM
OF
CONTROL SERA

it was found that the reported 1979 levels of both Aroclor 1254 and p,p'-DDE, in both the study population and the out-of-state controls, were all about 7-fold higher than the levels reported in 1976. Accordingly a number of tests were run in 1980-81 to find the origin of the discrepancy.

Table 7-2 presents the results of a series of analyses of a control serum, which contained only a few ppb each of Aroclor 1242, 1254 and DDE, where the analyst was requested to duplicate the extraction procedures used in 1976 (PE) and 1979 (MH) as closely as possible. The results suggested that the PE method might work a little better for 1242, and MH slightly better for 1254 and DDE, but none of the differences were statistically significant.

Table 7-3 presents the results of several series of analyses on control sera that had been deliberately spiked with known levels of Aroclor 1242, 1254, or DDE. The results were mixed. Method MH gave good recoveries with 1254 and DDE, but poor recoveries with 1242. Method PE gave poor recoveries with DDE and 1254 in one series of runs, but good recoveries of 1254 in another. In the latter, interestingly enough, there were considerable run-to-run variations in the recovery of the added spike which were not paralleled by variations in the levels of recovered DDE, which was present before spiking. Again, it was difficult to demonstrate a convincing difference between the two extraction procedures.

A few experiments were done using an alternative procedure which differed from the methanol-hexane method in the omission of the

TABLE 7-2. COMPARISON BETWEEN TRIPLICATE ANALYSES OF CONTROL SERUM BY PETROLEUM ETHER – FREEZE-BY-DRY-ICE (PE) AND METHANOL – HEXANE (MH) METHODS

Species	Method	N	$\bar{X}$ (ppb)	S	PE/MH
1242	PE	3	3.303	0.4508	
1242	MH	3	2.690	0.5475	1.23[a]
1254	PE	3	7.577	0.8909	
1254	MH	3	9.223	0.3175	0.82[a]
1254	MH	41	11.5[b]		
DDE	PE	3	8.290	1.189	
DDE	MH	3	8.883	0.2902	0.93[a]
DDE	MH	34	10.7[b]		

a. T-test of difference of means not significant, $p > .05$
b. Average of many other determinations on same sample

TABLE 7-3. RECOVERIES OF SPIKES ADDED TO CONTROL SERA USING PETROLEUM ETHER – FREEZE-BY-DRY-ICE (PE) AND METHANOL – HEXANE (MH) METHODS

Species	Method	N	Before Spike	Spike (ppb)	After Spike	% Spike Recovery	DDE Obs'd.
1242	MH	3	7.93	10.0	14.0	61	–
1254	PE	10	10.0	10.0	14.76	48	--
1254	PE	1	10.0	10.0	23.1	131	17.5
1254	PE	2	10.0	20.0	32.2	111	16.3
1254	PE	2	10.0	50.0	50.9	82	16.4
1254	PE	1	10.0	100.0	122.0	112	17.2
1254	MH	3	13.4	10.0	22.9	95	–
DDE	PE	10	12.11	10.0	17.17	52	–
DDE	MH	3	10.4	10.0	18.7	84	

methanol denaturation (step 2, Table 7-1) and the use of straight hexane rather than hexane-ether as the extractant. Duplicate analyses showed the recoveries of 1254 and DDE to be only 45% and 49% of those provided by the methanol-hexane method, and that these recoveries were not improved by repeating the hexane extractions. This "straight hexane" method was never used in our study, but has been occasionally used by others.

The 1979 DDE levels reported for both our control and study populations, and the 1242 and 1254 levels reported for our control populations were all in good agreement with the U.S. background levels of PCBs and DDE reported by others, indicating that there is no reason to question the 1979 analytical results. The source of the roughly 7-fold error in the 1976 data for 1254 and DDE is still unknown. Also unknown is whether the error also affected the 1976 results for Aroclor 1242 (As will be seen in the next Section, the latter tended to be <u>higher</u> than the 1979 levels in the controls and other lightly exposed persons, but a little lower in the study population as a whole.) Because of these uncertainties, we have been advised by the Raltech analyst to disregard all of the 1976 data on serum PCB levels until the nature of the error has been determined. Accordingly, all of the calculations of body burden, correlations with exposure levels, and relationships to clinical symptoms described in later sections of this report will be based upon the 1979 data.

Tests of Precision of Procedures Used

Table 7-4 shows the results of 24 replicate analyses of a control serum pool over a one-week period using the 1979 (MH) procedure. The coefficients of variation for the determinations of Aroclor 1242, 1254, 1260, and DDE were found to range between 13.7% and 26.8%.

In order to determine the linearity of the response, a 60 ml. pooled sample was prepared from measured portions of the sera of 12 highly exposed subjects. The Aroclor contents were taken as the average of values calculated from the weighted contributions of the 12 sera used and those obtained by triplicate analysis of the pool. The pool was then serially diluted twice with the Raltech Red Cross serum pool and once using distilled water, and the diluted samples analysed by the 1979 (methanol-hexane) procedure. The results for Aroclor 1242, 1254, and 1260 are shown as data points in Fig. 7-1. The regression found to fit these data points was

$$\log y = 0.0947 + 0.951 \log x$$

where y is the reported PCB value and x that calculated from the dilution used. Fig. 7-1 also shows the calculated regression line, the line of identity, and the positions of boundaries about the regression of the 95% confidence limits on individual measurements. The line of identity falls within the confidence limits.

Judging by the results of a recent unpublished round robin study of the performance of 11 commercial laboratories (including Raltech) in

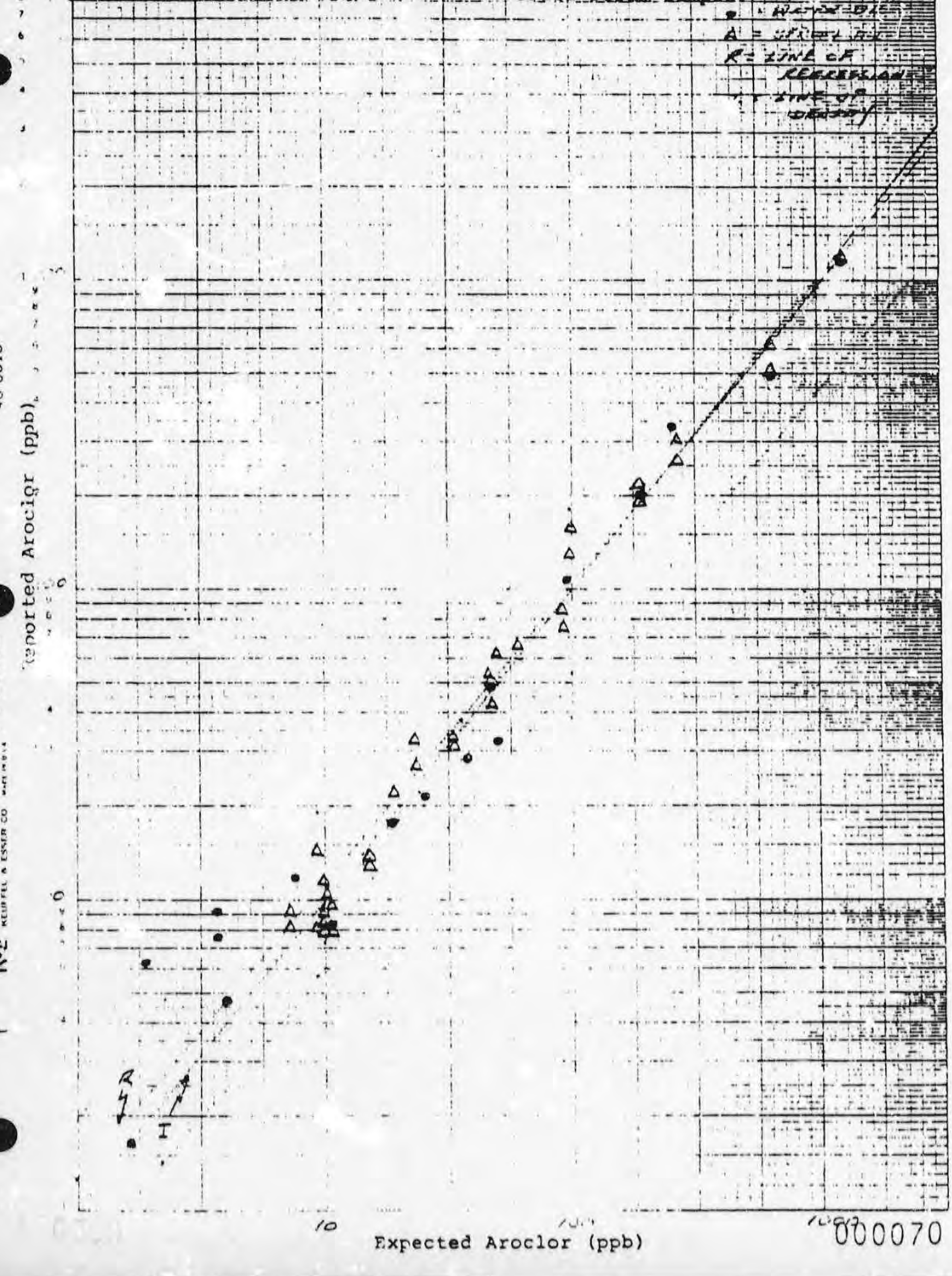
TABLE 7-4

PCB and DDE Levels in 24 Replicates of Control Serum

	Compounds Analyzed (ppb)			
Day	Aroclor 1242	Aroclor 1254	Aroclor 1260	DDE
1	4.73	8.07	a	9.47
	6.68	9.22	a	9.82
	8.86	11.1	a	10.4
	14.0	14.7	a	9.56
	10.7	17.9	a	10.1
	9.88	17.5	a	12.6
	10.7	14.6	a	10.4
	10.1	14.4	a	8.76
2	5.91	14.1	a	11.1
	6.91	16.0	a	13.9
	5.91	14.0	a	10.6
	6.03	13.4	a	11.4
3	8.46	16.3	10.4	12.9
	6.52	13.3	8.08	9.26
	6.34	13.1	7.69	8.77
	6.34	13.6	8.08	9.64
	7.05	13.6	7.31	9.97
	7.22	13.8	8.85	9.64
4	6.70	12.2	6.92	9.64
	7.58	14.0	8.08	10.5
5	8.41	9.81	4.62	7.48
	7.66	12.6	6.54	11.2
6	7.22	12.6	5.77	9.53
	10.5	12.9	6.15	11.4
Average	7.93 ± 2.13	13.45 ± 2.33	7.37 ± 1.52	10.34 ± 1.42
High	14.0	17.9	10.4	13.9
Low	4.73	8.07	4.62	7.48
CV%	26.8	17.3	20.6	13.7

a Aroclor 1260 not quantitated.

Figure 7-1. Comparisons Between Reported and Expected Aroclor 1242, 1254, and 1260 Concentrations Determined by the Methanol-Hexane Procedure on Serial Dilutions of a Pooled Serum Sample.



the analysis of PCBs in hexane, water, and fish samples, conducted by the New York State Department of Health, this level of precision in determinations of serum Aroclor should be considered as highly creditable, state-of-the-art, performance.

Ambiguities in Reporting Procedures Used

It should be noted that the PCB analyst faces some knotty problems in finding defensible ways to report his findings. The commercial PCBs all consist of complex mixtures of homologs and isomers, which give rise to complex, multi-peak gas chromatograms (Figs. 2-4 of Table 7-1). The electron capture detector gives markedly different responses for different PCB isomers, so that the relative heights of different peaks may be greatly different from the relative weight concentrations of the species producing those peaks. In environmental samples, there may be extraneous peaks from chlorinated pesticides, which obscure some of the PCB peaks, and partial biodegradation may have occurred, leading to peak distributions different from those in the standards (compare Figs. 2 and 5 of Table 7-1). A conventional solution to these problems is to report the collection of observed peak heights as a concentration of "Aroclor xxxx." What this parameter really denotes is the concentration of an Aroclor xxxx standard required to produce one or more peaks, the sum of whose heights is equal to that of selected (but frequently unspecified) peaks found at the corresponding retention times in the chromatogram of the sample. This operational procedure can, in principle, be conducted to any level of accuracy and precision. However, it is important to realize that a concentration reported as "Aroclor xxxx," or even the sums of concentrations so reported, cannot be equal to the total PCB concentration in the sample except in the special case where the isomer distribution in the sample is identical to that in the standard. These inequalities, which result in ambiguities in the actual levels of PCB's present even in samples where the "Aroclor xxxx" levels are accurately and precisely reported, are of two kinds:

The first, and more easily managed, results from the fact that the ranges of composition of the various Aroclors overlap, and the reporting procedure permits multiple reporting of the same peaks. Some sample calculations of the sort of confounding that can result, based on the peaks used by Raltech on the 1979 samples, are shown in Table 7-5. It is seen that if comparable amounts of lower and higher PCB's be present, the reporting of Aroclors 1242 and 1254 and 1260 will result in an approximately 2-fold overreporting of the total PCB in the sample. Such overreporting can be minimized by reporting only Aroclor 1242 and 1260. Alternatively, some investigators are getting away from the range-overlap problem by reporting their data as "lower PCBs" (LPCB) and "higher PCBs" (HPCB). The former corresponds to those isomers giving peaks before the DDE peak on the chromatogram, the latter to those giving later peaks. If the LPCB and HPCB values

TABLE 7-5. CALCULATED LEVELS OF VARIOUS AROCLORS THAT WOULD BE REPORTED FOR TYPICAL AROCLOR SAMPLES USING THE 1979 RALTECH SUM-OF-SELECTED-PEAK-HEIGHTS METHOD OF QUANTITATION

Composition of Sample	Reportable Level of Aroclor 1242	1254	1260	Sum
Pure Aro 1242, 100	100	10	5	115
Pure Aro 1254, 100	60	100	47	207
Pure Aro 1260, 100	22	143	100	265
1242, 100 + 1254, 100	162	111	52	325
1242, 100 + 1260, 100	120	160	106	386

be also determined by the sum-of-selected-peak-heights method, then in samples of the type being considered here, the LPCB and HPCB values should be fairly close to those for "Aroclor 1242" and "Aroclor 1260," respectively.

The second source of uncertainty arises when the distribution of isomers in the sample differs from that in the standard. Quite obviously, if the peaks selected for use in the sum-of-selected-peak-heights procedure happen to be those of the few isomers that persist after most of the other PCB isomers have been eliminated, then this procedure can considerably overstate the total amount of PCB present. Comparisons of the chromatograms of human sera (e.g., Table 7-1, Fig. 5) with those of the Aroclor standards (ibid., Figs. 2-4) suggests that there is a distinct possibility that this could be the case for the serum PCB data reported as Aroclor 1242, but not for that reported as 1260, and probably not that reported as 1254.

One possible way to avoid ambiguities resulting from variations in isomer distribution is to analyze the sample by the perchlorination procedure, which converts all isomers alike to decachlorobiphenyls for quantitation and reporting as total PCB. Unfortunately, that procedure also obliterates the distinction between LPCBs and HPCBs, which may be of clinical importance. In addition, in our hands at least, it has not yet performed satisfactorily on PCBs recovered from sera.

A more reliable alternative procedure would be to measure the height of every peak on the chromatogram, discard those corresponding to known pesticides or other environmental contaminants, divide each of the remaining (PCB) peaks by its published electron capture response factor, determine the ratio of each quotient to that for the corresponding peak in the standard and thence its individual concentration in the sample, and finally to add up all the concentrations for peaks in the range of interest to determine the total PCB present. Even with use of a computer to perform the calculations, this would be a fairly laborious procedure, and has not yet been applied to our chromatograms. However, until it is done, at least on representative samples, we cannot be sure whether the serum "Aroclor 1242" values, as conventionally reported, really do correspond to acceptable measures of absolute serum LPCB.

Meanwhile, we are proceding with various clinical studies and epidemiological correlations as described in later sections of this report. In all correlations made and described to date we have used, as measures of serum PCB levels, the 1979 values for "Aroclor 1242," "Aroclor 1254," and "Aroclor 1260" exactly as reported to us by Raltech. If and when it becomes possible to refine these somewhat ambiguous measures of PCB levels, we shall rename the parameters used, probably to something like LPCB and HPCB, and recalculate the data as required.

8. Serum PCB Findings

The reported distributions of serum Aroclor 1242, 1260, and DDE in our heavily exposed study population (Group 1) is displayed in Figure 8-1. It is seen that the data are log normally distributed and have approximately the same slopes on the cumulative percentage plots, indicating similarity in the standard deviations. Statistical descriptors of such data distributions for this study group and the out-of-state controls (Group 3) are summarized in Table 8-1.

In summarizing the 1976 data for DDE, where nearly 50% of the values were reported as $\leq$ 1 ppb, we used the maximum likelihood technique for modelling censored data (Section 14, below). The 1979 data for DDE Groups 1 and 3 exhibited arithmetic means of 13.1 and 14.4 respectively. These are shown in Table 8-2 to be similar to other DDE background value reported in the recent literature.

Figure 8-1. Distributions of Reported Serum PCB and DDE Measurements on Study Population (Group 1).

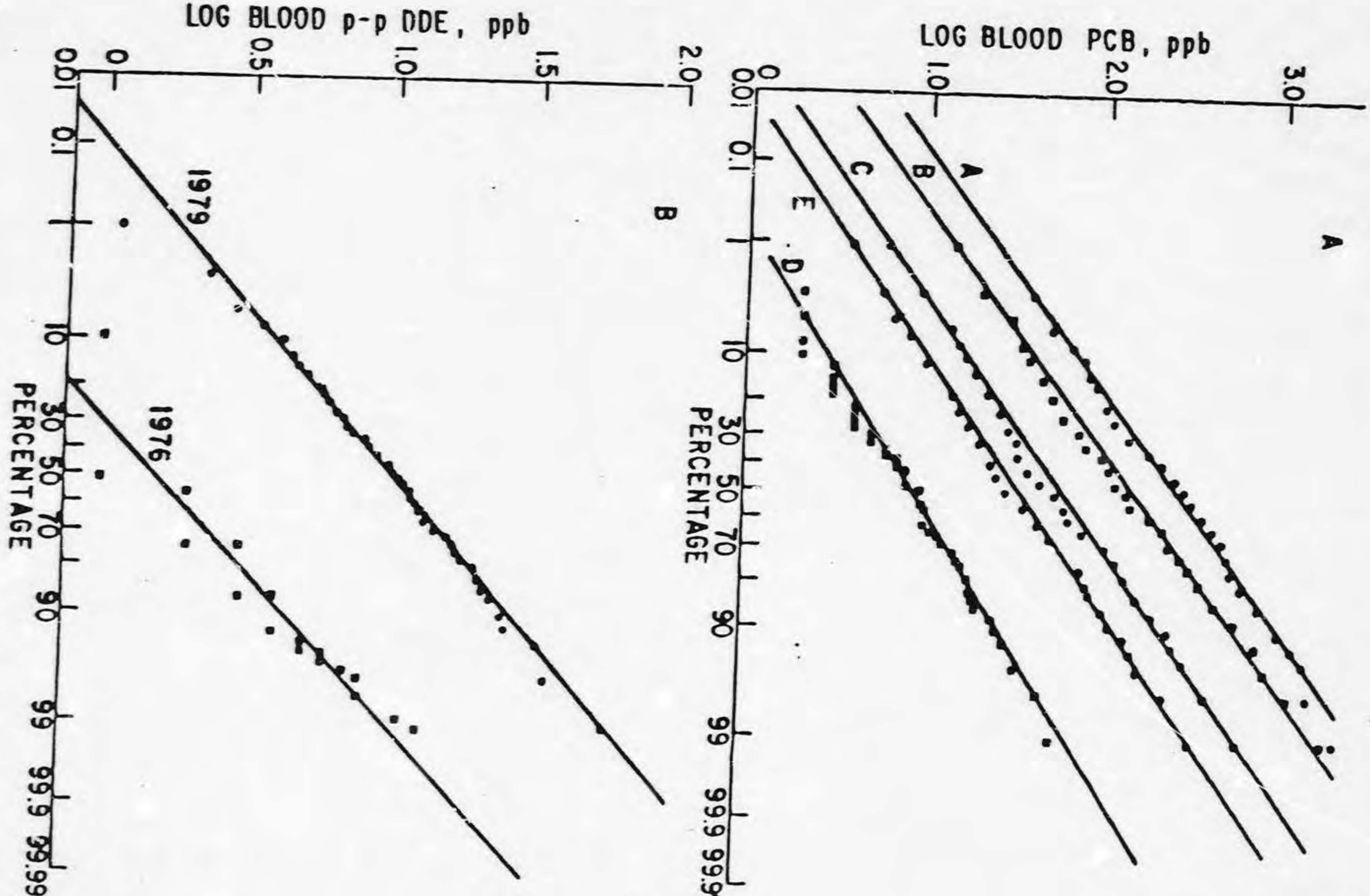


Figure 8-1

000077

TABLE 8-1. SUMMARY OF SERUM PCB AND DDE MEASUREMENTS ON STUDY AND CONTROL POPULATIONS

		Lognormal Distributions			Normal Distributions	
	N	log $\bar{X}$	log S	Geometric Mean (ppb)	$\bar{X}$ (ppb)	S
Study Population (Group 1)						
Aroclor 1242						
1976	184	2.18*	0.50	150*	283*	386
1979	172	2.44	0.48	276	458	486
Aroclor 1254						
1976	184	0.92*	0.40	8*	12.5*	12.9
1979	172	1.76	0.46	58	100	122
Aroclor 1260						
1979	144	1.53	0.44	34	56	64
p-p DDE						
1976	166	< 0.24*		< 1.8*	< 2.[illegible]*	
1979	172	1.00	0.34	10	13.1	10.6
Control (Group 3)						
Aroclor 1242						
1976	18	1.06*	0.07	11.4*	11.5*	1.9
1979	18	0.83	0.21	6.7	7.6	4.6
Aroclor 1254						
1976	18	0.25*	0.15	1.8*	1.9*	0.7
1979	18	1.13	0.23	13.4	15.5	9.9
Aroclor 1260						
1979	18	0.97	0.29	9.2	12.1	11.9
p-p DDE						
1976	16	< 0.19*		< 1.5*	< 1.6*	
1979	18	1.03	0.37	10.8	14.4	10.0

*The analyst has recommended that we disregard these data until the source of the error in the 1976 Aroclor 1254 and DDE data has been identified.

TABLE 8-2 REPORTED p,p'-DDE LEVELS IN HUMAN BLOOD

	p,p'-DDE, ppb (Arithmetic Means)	N	
Doguchi & Fukano (1975)	11.2 ± 4.5	14	Whole Blood
Curley & Kimbraugh (1969)	13.0 ± 1.5	10	Plasma, females
Dale, et al. (1966)	11.4 ± 2.1	10	Males, whole blood, no occp. exp.
	25.7 ± 4.3	10	Plasma
	19.8 ± 4.1	10	Serum
Wolff, et al. (1978)	12.9 ± 11.9	524	Dairy farmers (Michigan) serum
	11.4 ± 7.4	55	Farmers (Wisconsin) serum
	21.4 ± 18.1	56	Chemical workers (Michigan) serum
Morgan, et al. (1972)	87 (50 - 145)	10	Pesticide workers, plasma
This Study (1979)	13.1 ± 10.6	170	Capacitor workers (Upstate, NY) serum
	14.4 ± 10.0	18	Officer workers (Connecticut) serum

The distributions of the 1979 serum PCB levels among various subpopulations were also examined. Small, statistically insignificant differences in geometric mean values were found between the two plants, with slightly higher levels at Hudson Falls than at Ft. Edward (Aroclor 1242, 311 vs. 253 ppb; Aroclor 1254, 98 vs 42 ppb.) Females had slightly higher serum values than males, as expected because of their longer average service times and their participation in highly exposed jobs. Salaried administrative personnel generally had serum PCB levels in the lower deciles. The mean levels in the various employee subpopulations defined in Section 5 are listed in Table 8-4.

This Table shows that 1979 serum Aroclor 1242 levels were signifantly above background levels for all worker groups in the plants, including those employed since discontinuance of PCB use in 1977. Those assigned to study group 1 (direct exposure in 1976) subgroups L and M (low and medium exposure) proved to be statistically indistinguishable from each other, and hence were lumped together. The geometric mean levels for plant employees with no direct exposure, with low to medium direct exposure, and with heavy direct exposure were 50.4, 179, and 676 ppb, respectively, corresponding to 7.5, 25.7, and 101 times the levels in the controls.

The 1979 serum Aroclor 1260 levels were above background in the directly exposed groups, again with significant differences between those having low-medium vs. high exposures, but not significantly above background in the employees with only indirect exposure or those employed since 1977. (Table 8-4) This may indicate that uptake of the more highly chlorinated (and hence much less volatile) Aroclors requires direct physical contact.

TABLE 8-4 1979 SERUM PCB LEVELS OF VARIOUS HUDSON FALLS-FT. EDWARD WORKER GROUPS

		Group No.	Aroclor 1242 GM ppb	Aroclor 1242 In-Plant Service Yrs	Aroclor 1242 N	Aroclor 1242 Ratio to Background	Aroclor 1260 GM ppb	Aroclor 1260 In-Plant Service Yrs	Aroclor 1260 N	Aroclor 1260 Ratio to Background	Net Accumulation Rate (ppb/yr) (Over Background) Aro 1242	Net Accumulation Rate (ppb/yr) (Over Background) Aro 1260	
No Exposure (Non-plant control)			3	6.7	0	18	1.0	9.2	0	18	1.0	0	0
Employed, not Occup. Exposed*			4	50.4	23.6	18	7.5	11.3	23.6	18	1.0	1.85	0
Low Exposure* • •	 Continuous at zone periphery Short, irregular high exposure		1 (L) (M)	179	16.3	102	25.7	26	16.6	86	2.6	10.6	0.96
Exposed Pop. Mean*			1	269	16.5	147	39.2	33	16.8	123	3.3	15.9	1.37
High Exposure* •	 Continuous in exposure zone		1 (M)	676	17.0	45	101	59	17.4	37	5.9	39.4	2.82
Employed since PCB Ban: Works in treat area**		5	28.3	2	16	3.2	7.8	2	16	1.0	10.8	0	

*Assumes continuous employment in exposed jobs

**Average area air level (1/78 - 12/80) = 57.3 $\mu g/m^3$

9. Calculations of the PCB Body Burden

In this Section we shall describe and explain a method for calculating the total body burden of PCBs, using only the sorts of data already described. This method is based on the assertions that: (a) the concentrations of PCBs in adipose tissue fat can be calculated from data on serum PCBs and serum lipids; (b) the total mass of fat in the body can be estimated from body weight and age, using the empirical relations given by Moore; and (c) the total mass of PCB in the body may be calculated as the product of the PCB concentration in the fat multiplied by the total mass of fat present. These assertions will be discussed in turn.

A. Distribution of PCBs Between Blood and Adipose Tissue

Virtually all of the PCBs and other non-polar halogenated hydrocarbons present in the body are found to be localized in adipose tissue. When various organs are examined individually, the chlorocarbon concentrations are found to be quite closely proportional to their lipid contents, except in the case of brain tissue, which is predominantly phospholipid. It has been found, however, that this discrepancy may be removed and the correlation between chlorinated hydrocarbon levels and lipid contents of various organs, including the blood, be further improved if the lipid content be expressed as "extractable lipid" (which includes the weakly polar triglycerides, cholesterol, etc. but not the strongly polar phospholipids). The "extractable lipid" contents of various adipose tissues examined during the course of chlorinated hydrocarbon distribution studies were 74±17 percent (1). Such correlations have led to the conclusion that these chlorinated hydrocarbons, which are characteristically water-insoluble, lipid-soluble species are primarily localized in the non-polar (non-structural) lipid domains of adipose tissue, and at least in equilibrated individua are to be found at equal levels in all such lipid domains. This conclusion has led, in turn, to the practice of expressing the results of analyses of adipose tissue for species such as PCB's in terms of ppm relative to extractable fat, rather than relative to total tissue weight.

Within the blood its lf considerable evidence indicates that PCB-like species are carried by the serum lipoproteins within their non-polar (lipid) domains (2). They are probably not carried by the short-lived chylomicrons, as evidenced by studies on p,p'-DDE by Morgan et al (3). Only 3-5 percent of the radioactivity following labelled PCB injection in rats is associated with the red cell (4)

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1. Morgan, D.P., and C.C. Roan. Chlorinated Hydrocarbon Pesticides in Human Tissues, Arch. Environ. Health 20:452-457 (197[illegible]

2. Skalsky, H.L., Fariss, M.W., Blanke, R.V. and P.S. Guzelian. The role of plasma proteins in the transport and distribution of chlorecone (Kepone[R]) and other polyhalogenated hydrocarbons. Ann. N.Y. Acad. Sci. 320: 231-237, 1979.

3. Morgan, D.P., Roan, C.C. and E.H. Paschal. Transport of DDT, DDE and Dieldrin in human blood. Bull. Environ. Contam. Toxicol. 8: 321-326, 1972.

4. PCB Poisoning and Pollution. Ed. K. Higuchi. Academic Press, New York 1946.

and such activity could be due to the serum still adherent to the washed cells (1). Thus, for chylomicron-free blood (taken from a fasting individual) we should expect the PCB level in the lipid domains of the serum lipoprotein molecules to be equal to that in the lipid domains of the adipose tissue, and hence the PCB distribution between adipose tissue fat and serum to be determined by the concentration of the appropriate lipid domains in the serum.

The reported adipose tissue fat vs serum distribution coefficients for halogenated hydrocarbons all seem to cluster near 300. The data of Karppanen and Kolho (5) for PCB in Finnish capacitor workers averaged 312; for PBB Landrigan et al (6) calculated 362.8; for p,p'-DDE a value of 209 has been found (1).

Wolff et al (7) investigated adipose tissue-serum partition for various PCB isomers. The lowest partition was found for the 2,5-chlorine substitutions (<100). PCB congeners with 3,4-(or 2,3,4-) chlorine substitutions on one or both biphenyl rings or with 2,4- (or 2,3,4-) substitutions on the opposing ring had partitions from 100-190. Partitions greater than 200 were found for congeners with

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5. Karppanen, E. and L. Kolho. The concentration of PCB in human blood and adipose tissue in three different research groups. In PCB Conference II, Stockholm, 1972. Nat. Swedish Environ. Protection Board Pub. 1973: 4E:124-128.

6. Landrigan, P.J., Wilcox, Jr., W.R., Silva, Jr., J. et al. Cohort study of Michigan residents exposed to polybrominated biphenyls: epidemiologic and immunologic findings. In: Ann. N.Y. Acad. Sci. 320: 284-294, 1979.

7. Wolff, M.S., Fischbein, A., Rosenman, K. and I. Selikoff. Comparison of polychlorinated residues in humans with varying exposures. 182nd Annual Meeting ACS, New York, Aug. 1981. Abstract pgs 170-171.

2,4- (or 2,3,4-) chlorine on both rings or in 2 compounds with 4-substitution on one ring. The low partition coefficients found for the 2,5-substituted and certain other isomers were attributed to the very rapid metabolism of these isomers in the liver, leading to incomplete equilibration with the fatty tissue. For the majority of the isomers present in the capacitor workers bodies, the adipose tissue/serum ratios were above 200, again corresponding to about 300 in adipose tissue fat/serum ratio.

The individual data points used in determining PCB distribution coefficients are shown in Figure 9-1. The data from Wolff (to be published) were determined by capillary gas chromatography; they are plotted using closed circles for L-PCB and open circles for H-PCB. The data of Karppanen and Kolho (5) are the solid squares. Two data points due to Inoue (triangles) were taken from Wasserman's tables (8).

Figure 9.1 presents the entire data on log-log coordinates, but Wolff found that her own data were better described by the linear regressions

H-PCB: Adipose PCB = 2.37 + 0.192 Plasma PCB (r=0.70; n=26)

L-PCB: Adipose PCB = 6.3 + 0.183 Plasma PCB (r=0.98; n=25)

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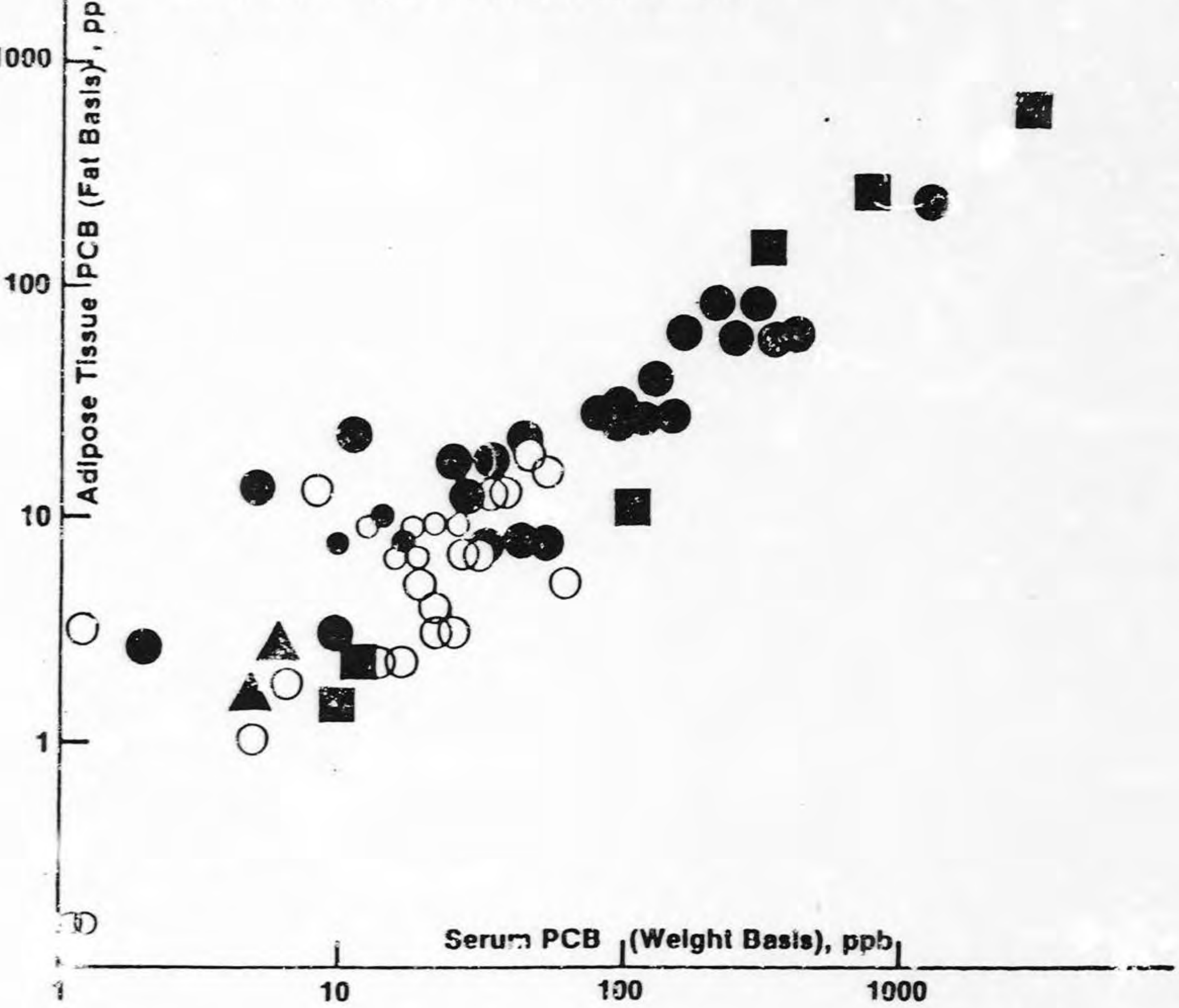
8. Wasserman, M., Wasserman, D., Cucos, S., and J. H. Miller. World PCB Map: Storage and effects in man and his biological environment in the 1970s. Ann. N.Y. Acad. Sci. 320: 69-124, 1979.

FIGURE 1

Figure 9-1. Relationships Between Individual Adipose Tissue and Serum PCB Levels. Symbols identified in text.



In Figure 9-1 all the data are for individual cases. The use of arithmetic means of population data produce spurious relations because of serious skewing of the distributions.

Now, if PCBs be distributed equally throughout the available lipid pools of the body, then at equilibrium:

$$\frac{\text{Adipose Tissue PCBs}}{\text{Adipose Tissue Dilutable Lipid}} = \frac{\text{Serum PCBs}}{\text{Serum Dilutable Lipid}}$$

where the term "dilutable lipid" has been used to designate the mass of the lipid domain available for dilution by PCB (e.g. until the PCB has reached the same concentrations in all such domains).

In Figure 9-2 the data of Figure 9-1 are used to calculate this "serum dilutable lipid" (which turns out to be numerically equal to the reciprocal of the partition coefficient previously discussed) for each individual data pair. The mean value found was 297 mgms/100 grams. The regression curve with 95 percent confidence limits is also shown. The slope of the regression is not significantly different from zero, indicating the apparent size of the serum dilutable lipid phase to be independent of the level of PCB present.

In order to determine how the levels of this serum PCB-dilutable lipid might compare with those of the more conventional serum lipid measurements, we examined the various lipid levels in each of our population of 194 directly-exposed capacitor workers, and also the dependence of such lipid levels on the measure of PCB activity (i.e., chemical potential) that would be provided by the ratio of the serum

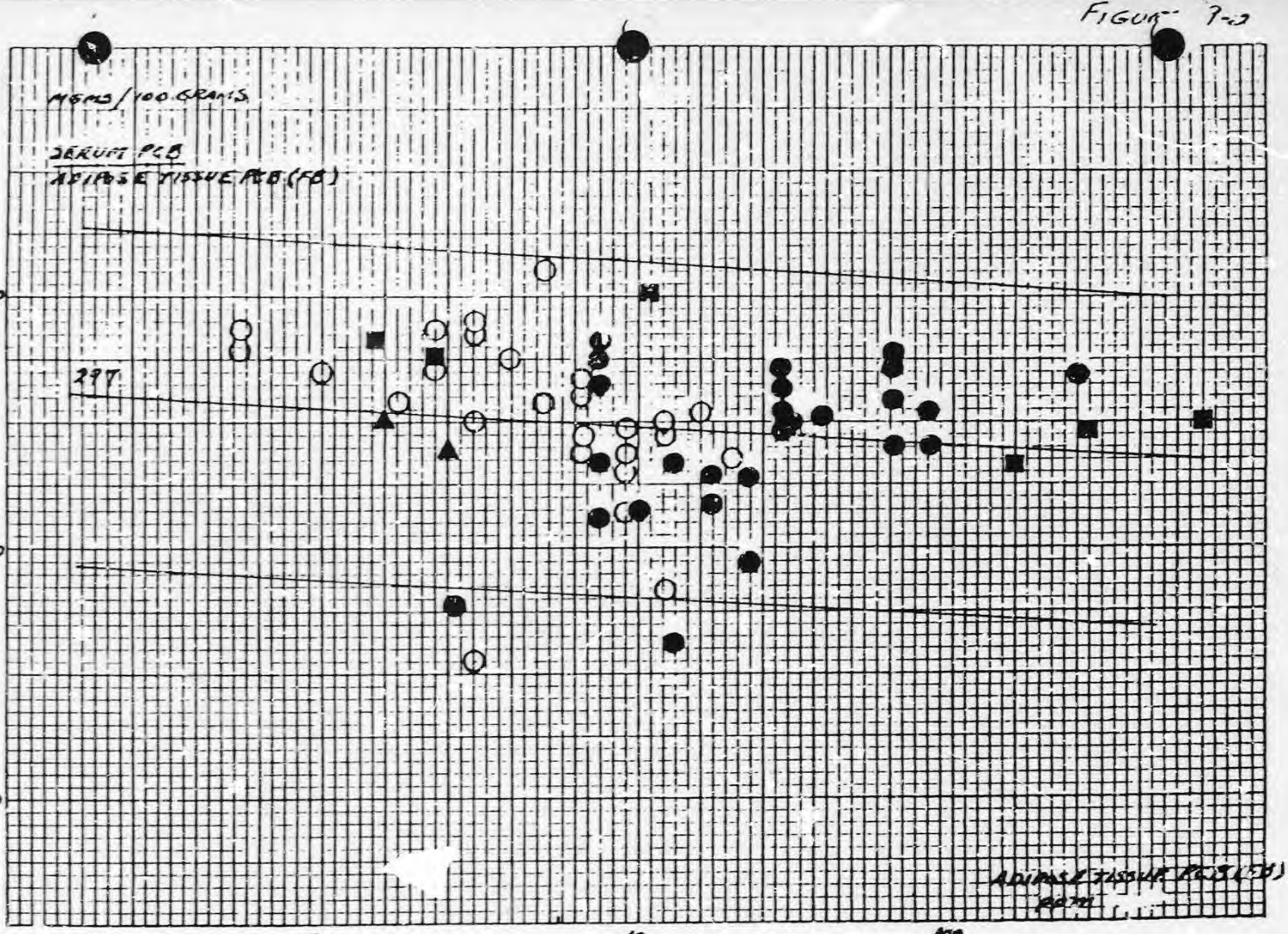
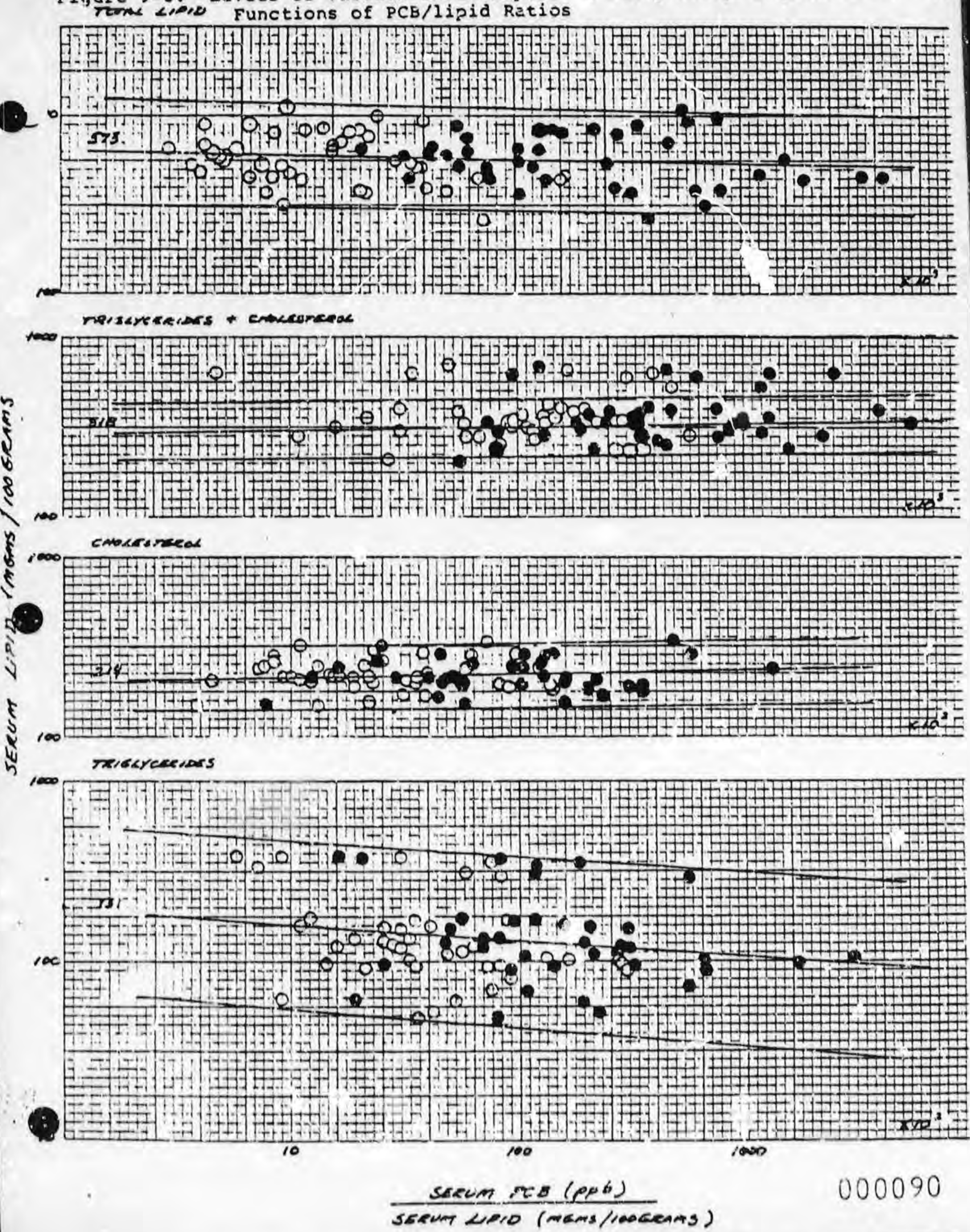


Figure 9-2. Calculated Serum Levels of PCB-Dilutable Lipid Domains for Individuals Having Various Levels of Adipose Tissue PCB.

PCB level to that of that particular lipid. The results are shown in Figure 9-3. It was apparent that there were no significant trends with respect to the more plausible measures of PCB activity, and hence that the overall average lipid levels could be taken as meaningful, PCB-independent parameters. These overall mean levels (all in mg/100 ml) were 573 for total serum lipids, 350 for the sum of serum cholesterol plus serum triglyceride when cases of hyperlipidemia were included, or 318 when they were omitted, 219 for serum cholesterol, and 131 for serum triglycerides. Quite obviously, the sum of serum triglyceride plus cholesterol (318 mg/100 ml) provided the best empirical measure of the average size of the PCB-dilutable lipid microphase (297 mg/100 ml). This is as would be expected on chemical grounds, since it is known that the triglycerides, cholesterol, and cholesterol esters (reported together as "cholesterol" in the analysis) are present as an essentially liquid microphase in the micelle-like lipoproteins, whereas the other constituents of "total serum lipid," such as the free fatty acids and the phospholipids, are present in more highly organized structures that would be less likely to accommodate the bulky PCB molecules.

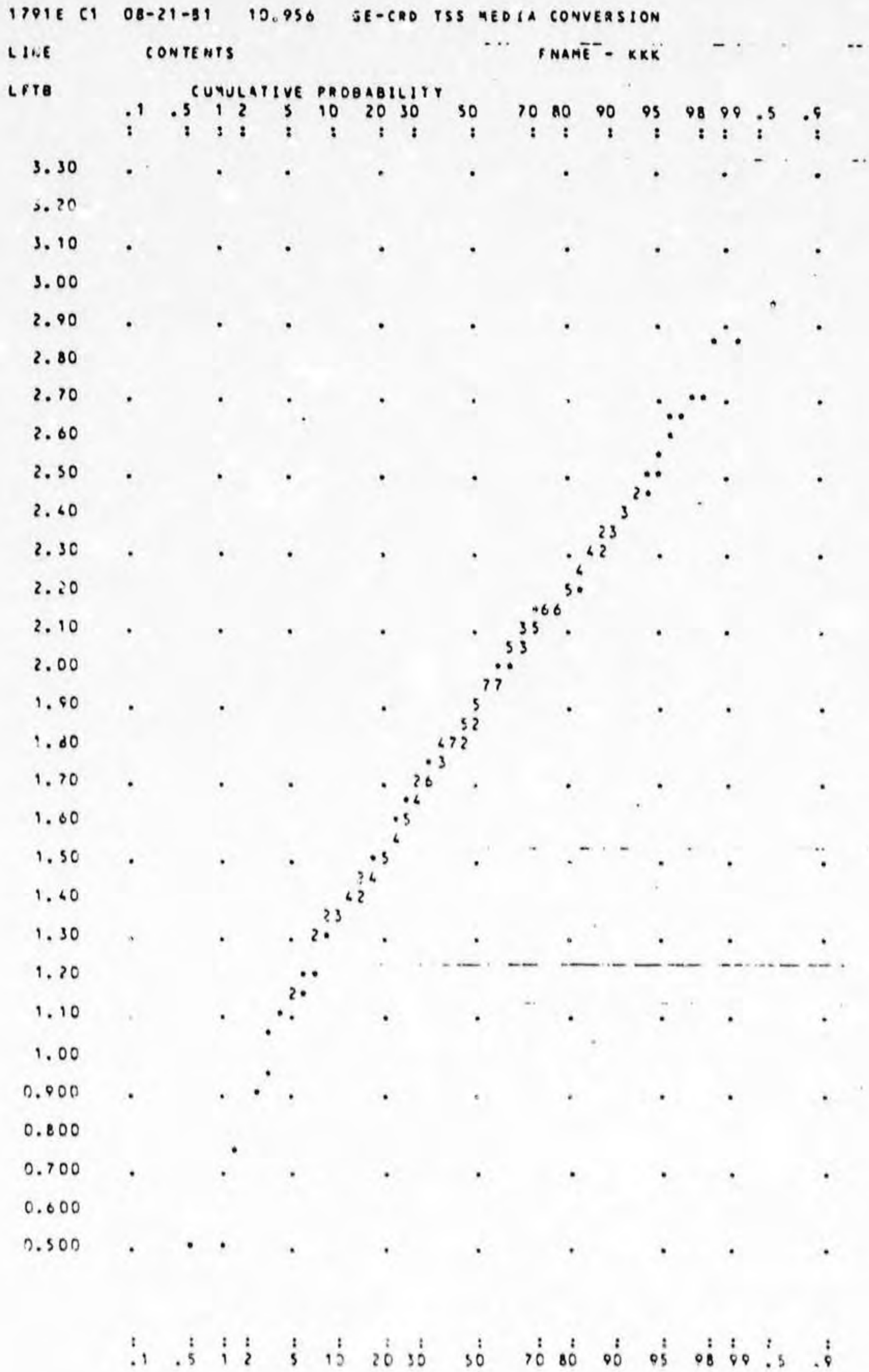
Having concluded that the sum of serum triglyceride plus serum cholesterol presents an empirical measure of serum PCB-dilutable lipid, we can use this quantity, plus the measured serum PCB level, to calculate the adipose tissue fat PCB level according to the above equation for any individual on whom we have data on serum triglycerides, cholesterol, and PCBs. Fig. 9-4 shows the calculated adipose tissue

Figure 9-3. Levels of Various Serum Lipids in Study Group 1, plotted as Functions of PCB/lipid Ratios



000090

Figure 9-4. Distributions of Calculated Adipose Tissue Fat PCB Levels in Directly-Exposed Capacitor Workers (Study Group 2).



fat PCB levels thus calculated for our Study Group 1 plotted on cumulative percentage coordinates. The data were found to be log normally distributed with a geometric mean of 74 ppm, and a range of values (5th to 95th percentile) of 14.4 to 379 ppm.

Discussion

To a first approximation, the correlation of the "serum PCB-dilutable lipids" with the sum of the triglycerides plus cholesterol is biochemically plausible, and consistent with the fact that brain tissue (mostly organized phospholipid)does not pick up chlorinated hydrocarbons the way adipose tissue does (1). We suspect, though that a more precise measure of the "serum PCB-dilutable lipids" would probably consist of some sum such as triglycerides + $\underline{x}$ cholesterol + $\underline{y}$ phospholipid where $\underline{x}$ might not be exactly 1.0 and $\underline{y}$ might not be exactly 0.0. In order to define the parameters $\underline{x}$ and $\underline{y}$ it would be necessary to have data of tissue fat PCBs, serum PCBs, serum triglycerides, serum cholesterol, and serum phospholipids on a large number of individuals, and then perform a multiple regression analysis. It is unlikely, however, that the resulting refinements in the calculation of tissue fat PCB levels from serum PCB levels would remove more than a small fraction of the imprecision contributed by the latter data. For the moment, we have an empirical method for calculating adipose tissue fat PCB levels that can be shown to give the right results on the average, and have no basis for believing that it should give seriously inaccurate results for any individual where there has been adequate time for equilibration of the PCB body burden among the various lipid compartments.

We should also point out that since PCB is predominantly carried within liquid lipid microphases in the body, the only meaningful measure of its potential for chemical and pharmacological activity is its concentration in such phases, not that in either the serum, individual tissues, or body as a whole. Thus, the calculation of tissue fat PCB levels provides us with a parameter that can be used not only in calculations of total body burden, but also in studies of the correlations between body PCBs and observable medical phenomena.

B. Calculation of Total Body Fat

The study of body composition, in particular the measurement of total body fat, has employed a wide variety of approaches. These include cadaver analysis, determinations of body density, those of total body water, combined density and body water determinations, absorption of nontoxic fat-soluble gases, whole body counting of radioisotopic potassium (K^{40}), measurement of multiple parameters by dilution techniques, measurement of subcutaneous fat by roentgenography, and caliper measurements of skinfold thickness. Because most of the methods considered best are technically complicated, and demand skilled personnel and equipment only available in special laboratories, they are not suitable for public health studies dealing with large groups of people. For this reason much attention has been devoted to the development of skinfold thickness measurements, which have resulted in an extensive literature (9,10,11,12).

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9. Grande, F. Assessment of Body Fat in Man. In Obesity in Perspective. Proceedings of the Conference. Ed. G.A. Gray et al. U.S. Printing Office. Stock No. 017-053-00046-9, pg. 189-203.

In our study skinfold thickness was not measured. In order to calculate body fat we have used the empirical equation developed by Moore et al (13) based upon total body water (TBW) measurements. These relations are as follows:

$$\text{Males: } \frac{TBW}{B.Wt} \times 100 = 79.45 - 0.24\,(B.Wt.) - 0.15\,(Age)$$

$$\text{Females: } \frac{TBW}{B.Wt} \times 100 = 79.81 - 0.26\,(B.Wt.) - 0.12\,(Age)$$

where body weight is in kg. and age is in years.

For the well-hydrated subject the fat-free body weight (FFB) is

$$FFB = \frac{TBW}{0.732}$$

based on the assumptions that fat is anhydrous and that the lean body is 73.2 percent water.

Body fat (kgs) is given by:

$$Fat = B.Wt - FFB$$

A basic premise of the calculation of body fat by this method is the assumption of adequate hydration in the individual. Sodium,

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Keys, A. and Brozek, J. Body fat in man. Phys. Rev. 33: 245-325, 1953.

11. Steinkamp, R.C., Cohen, N.L., Siri, W.E. et al. Measurements of body fat and related factors in normal adults. I. Introduction and Methodology. J. Chron. Dis. 18: 1279-1289, 1965.

12. Ibid. II. A simple clinical method to estimate body fat and lean body mass. J. Chron. Dis. 18: 1291-1307, 1965.

13. Moore, F.D., Olesen, K.H., McMurray, J.D. et al. The Body Cell Mass and its Supporting Environment. W.B. Saunders Co., Philadelphia, 1963.

potassium and chloride levels in our subjects were generally within normal limits. Serum osmolality was calculated using the relation (14):

$$2(\text{Serum [Na]} + [\text{K}]) + \frac{[\text{BUN}]}{2.8} + \frac{[\text{Glucose}]}{18}$$

The mean value was 294.2 mOsm/kg water, which is within normal limits. A plot of osmolality vs. serum Na concentration (mean 139.5 mEq/liter) is shown in Figure 9.5.

Siri (15) has described the analytical errors applicable to this calculation of body fat. ($\pm$ 3.6 percent of total body weight) The total body water results of Moore et al. indicate 95 percent confidence limits as $\pm$ 15 percent of the mean. Moore et al. point out that a linear regression between body weight and body fat underestimates fat at both low and high body weights. The parabolic expression given above satisfies the requirement that fat be present even at very low body weights (unlike linear regression which has a negative body fat intercept) and that fat increases disproportionally rapidly with increasing body weight, which conforms with clinical experience.

Figure 9-6 shows body fat in our population as a percent of body weight on cumulative percentage coordinates. The mean value is near 28 percent with a range of 19 to 38 (5th and 95th percentiles). The mean is near Moore's normal range for the average body weight and age of our population.

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14. Merck Manual, 13th Ed., March & Co., Rahway, N.J. 1977, p. 1184.

15. Siri, W.E. The gross composition of the body. Advan. Biol. and Med. Physics 4:229-280, 1956.

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2370C C1  05-27-81    15.854   GE-CRD TSS MEDIA CONVERSION

LINE         CONTENTS                            FNAME - OUTPUT

CROSSPLOT (NA79; OSMOL)

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NO.  CELL
IN   LOWER        280.00     290.00     300.00
ROW  ENDPT              285.00     295.00     305.00
                  <.+....+....+....+....+....+....+>
          ABOVE
         145.50+
  2      145.00+                            1     1
         144.50+
  3      144.00+                           111.
         143.50+
  8      143.00+                     1  2113
         142.50+
 21      142.00+                       2A6 21
         141.50+
 25      141.00+                 214643211 1
         140.50+
 23      140.00+              1434662 2
         139.50+
 28      139.00+             3 A74211
         138.50+
 31      138.00+         1123A332  1
         137.50+
 10      137.00+          312121
         136.50+
  5      136.00+        12   11
         135.50+
 11      135.00+    2411 2 1
         134.50+
         134.00+
         133.50+
  1      133.00+  1
         132.50+
  1      132.00+ 1
          BELOW+
                  <.+....+....+....+....+....+....+>
        NO.           2   3  15   9   5   6
        IN          1   4   6  11  12  16   4
        COL.         1   1   3  18  15   8   1   1
                          2   7  14   7   2 174 TOTAL

  20 CASES WITH MISSING VALUES OMITTED FROM THE ABOVE.

15.847 O'CLOCK; PROCESSOR=   0.4 SEC; TOTAL=  50.3 SEC

STOP
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135 - 145

Figure 9-5. Relationship Between Serum Sodium and Serum Osmolality in PCB-Exposed Capacitor Workers (Group 1 .

25850 C1 02-26-81 14.926 GE-CRD TSS MEDIA CONVERSION

LINE CONTENTS FNAME - BFPLOTS

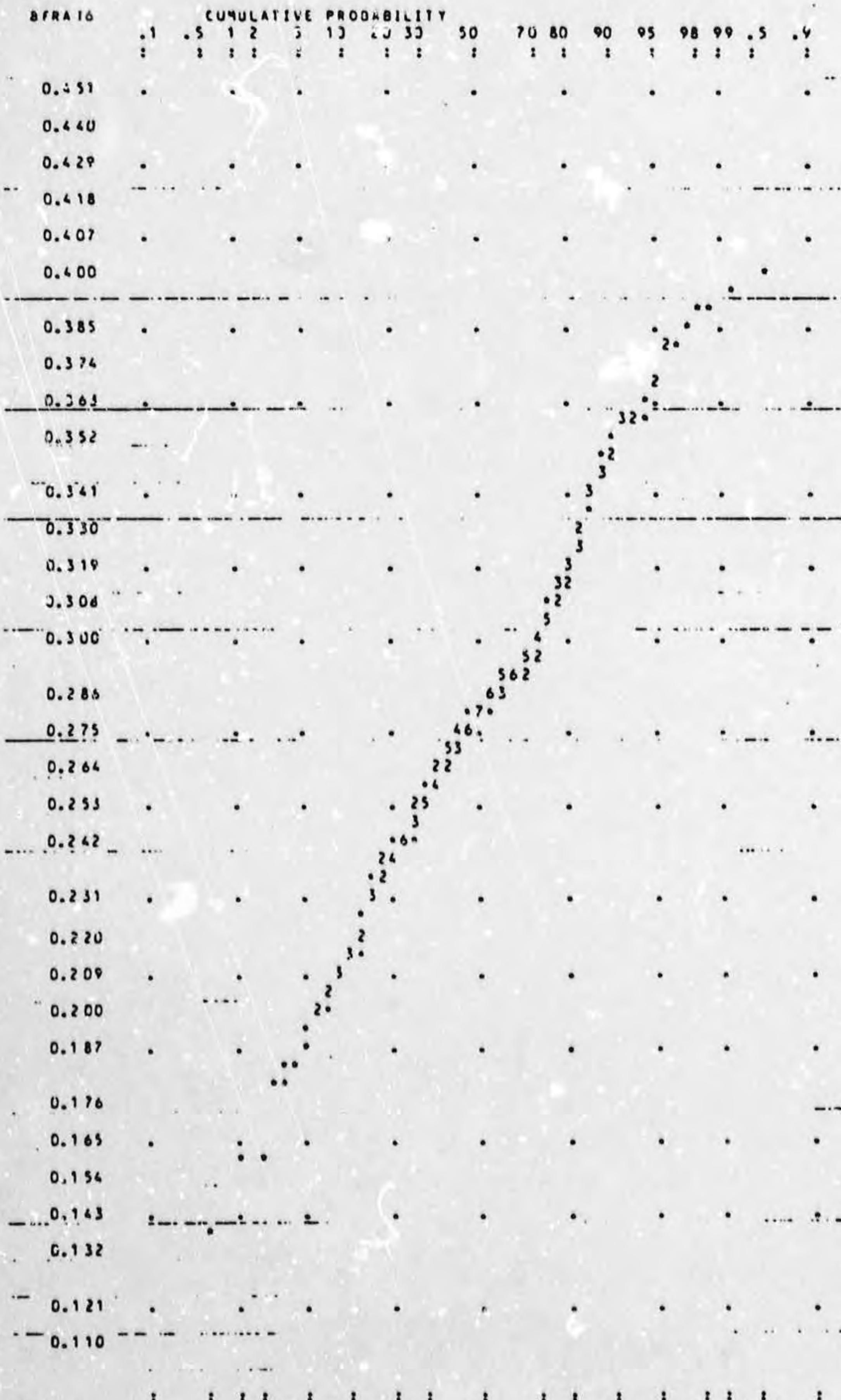


Figure 9-6. Body Fat as a Fraction of Total Body Weight in a Population of PCB-Exposed Capacitor Workers (Group 1).

I a comparison of various methods with his procedure, Steinkamp et al (11,12) found significant correlation coefficients which varied between 0.707 and 0.956 in the five subject groups studied. The Moore method compared favorably with other procedures based on anthropometry.

C. Calculation of PCB Body Burdens

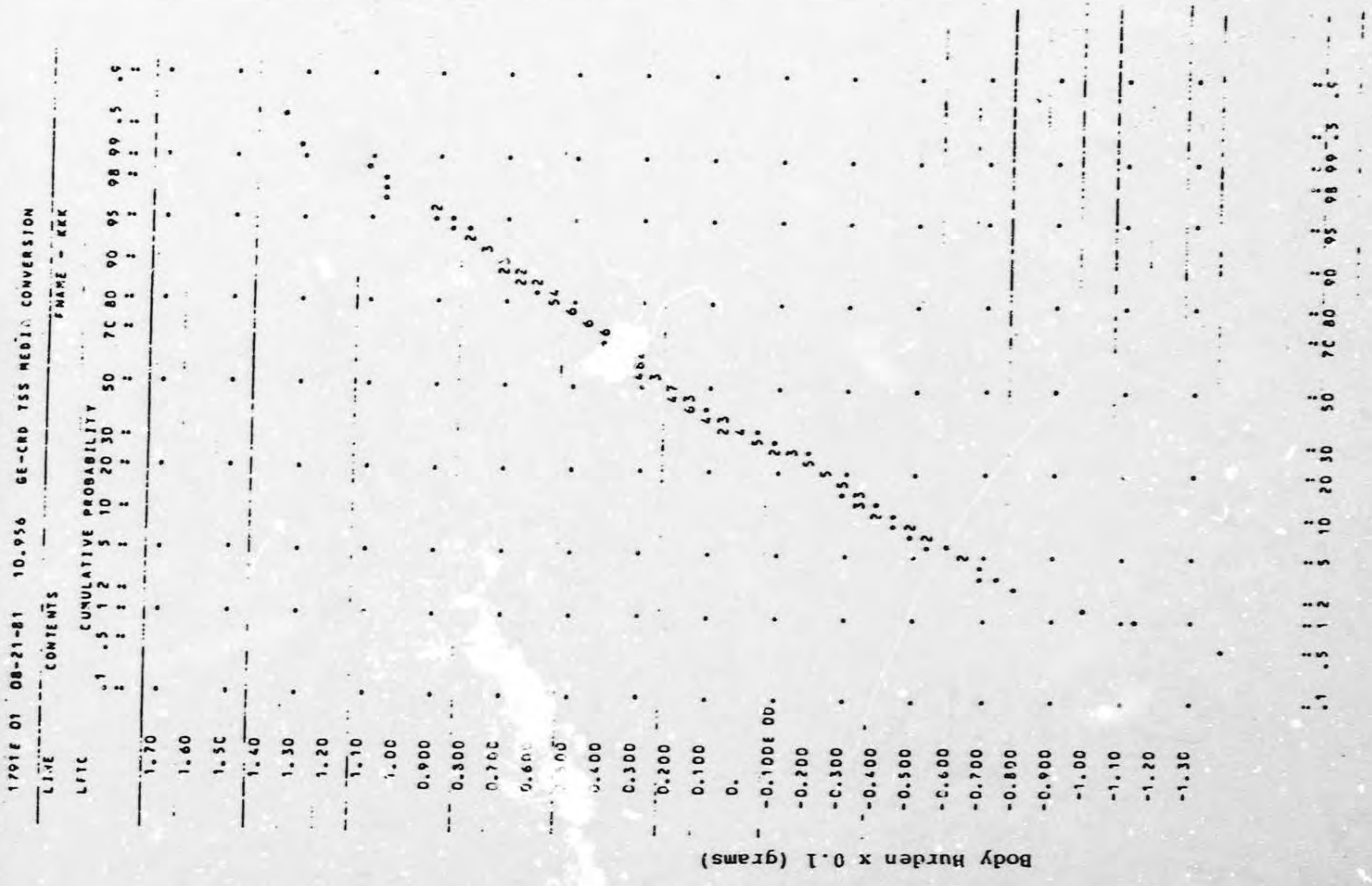
Knowing that virtually all the PCB in the body is sequestered in fatty tissue, and having developed procedures for calculating both the ratio of PCB to fat in such tissues and also the total amount of fat in the body, we have only to multiply the last two of these parameters to determine the total amount of PCB in the body. This can conveniently be done from the primary data using the equation:

$$\text{PCB Body Burden (grams)} = \frac{\text{Serum PCB(ppb)}}{\text{Serum tri + chol}\left(\frac{\text{mgms}}{100\text{ ml}}\right)} \times \text{B.wt(kgs)} \times 0.1024$$

The factor 0.1024 corrects the serum lipids to grams/gram and the other units to grams.

Figure 9.7 shows the range of body burdens for the lower homologs (as Aroclor 1242) in the study population for 1979. The data were found to be lognormally distributed with a geometric mean of 1.53 grams and 5th and 95th percentiles at 0.26 and 9.1 grams. The highest value was 22 grams, the lowest near 0.04 grams. The geometric mean for the higher homologs (as Aroclor 1260) was 0.02 grams and ranged between 0.004 and 0.13 grams. In contrast the mean body burden in the control population (Group 4) was 40 mgms for Aroclor 1242 and 55 mgms for Aroclor 1260.

Figure 9-7. Body Burdens of PCB's Analytically Reported as Aroclor 1242 in a Population of Directly Exposed Capacitor Workers (Group 1) as Measured in November, 1979.



Discussion

Assuming equilibration of the PCB in the body, there are still four known sources of error in the calculation of PCB body burden described here. In decreasing order of estimated importance, these are:

(1) Ambiguity in absolute amount of lower PCBs corresponding to that analytically reported as serum "Aroclor 1242." There is a smaller ambiguity in the absolute amount of higher PCB's corresponding to "Aroclor 1260."

(2). Imprecision in individual measurements of serum Aroclor 1242, 1254, or 1260.

(3) Inaccuracy in the estimates of total body fat by the Moore equation.

(4) Inaccuracy in the estimate of serum PCB-dilutable lipid as the sum of serum triglyceride and serum cholesterol.

The importance of error sources (3) and (4) is believed to be small in relation to (1) and (2), as already indicated. Source (2), of course, is of major concern in the appraisal of single measurements, but not in that of multiple measurements or group averages. Source (1), the ambiguity resulting from the comparison of a few peak heights in gas chromatograms of partially metabolized PCBs with those in unmetabolized standards, has not been resolved at this time. It is our present opinion, though, that the values of lower PCB body burdens calculated from our available Aroclor 1242 data, and reported in Figure 9-7, represent upper limits on the quantities of lower PCBs actually present as body burdens in 1979, but lower limits on the total quantities taken up during the preceding periods of exposure. Conversely, we suspect that the "Aroclor 1260" levels may somewhat understate the actual burdens of higher PCBs.

Even with such caveats as to the certainty of the data, they contrast strikingly with the estimates of PCB body burdens and uptakes reported by the Japanese investigators of the 1968 Yusho episode (poisoning by a PCB-PCDF-PCQ mixture, which we estimate to have contained 43-50% of undegraded Kanechlor 400 type PCB). They estimated that the minimum uptake required for the production of toxic symptoms was 0.5 grams of the mixture, corresponding to 0.22-0.25 g. of the PCB itself, and that the average victim had ingested 2.0 g. of the mixture, corresponding to 0.88-1.0 g. of PCB. Scattered adipose tissue fat PCB data obtained from the victims during the first year after ingestion indicated levels of 13 to 76 ppm (4), corresponding to body burdens of 0.15 to 0.85 g. (The total body fat in the Japanese Yusho population averaged about 11 kg, or 20% of body weight; i.e., approximately one-half that calculated for our worker population). Blood PCB levels taken five years after ingestion indicated the body burden to be in the background range (about 0.03 g.) In short, it would appear that the average capacitor worker in our group had taken up at least twice as much PCB as the average Japanese Yusho victim, and in 1979 was carrying a body burden that might have been up to 50 times as much as that being carried by the Yusho victims 5 years after exposure.

10. Relation of PCB Uptake to Exposure

At present, we have no definitive information on the relationships between occupational exposure and PCB uptake, but we do have several types of preliminary data indicative of the ultimate forms that such relationships may assume. These will be presented in turn.

In Table 10-1 we show again the serum PCB levels for our different study groups and call attention to the uptake estimates. These have been calculated in two ways: as the ratio of the observed serum geometric mean to the background (control) level and as the net accumulation (ppb/yr).

In Table 10-2 the serum Aroclor 1242 levels obtained in 1979 for 121 employees are correlated with job exposure in 1975 as measured by area air levels at the time of PCB use in manufacturing. During the 1975 period area air levels of Aroclor 1242 in the workplace varied from 200 to 2000 $\mu g/m^3$ with a geometric mean near 700 $\mu g/m^3$. A substantial period elapsed between air and serum measurements, which included the PCB ban, but the high body burdens, the potential for continued uptake from residual PCBs and the apparent general retention of significant serum levels (as measured in 1979) allow some preliminary analysis.

Net uptakes for the job categories in Table 10-1 were estimated as the ratios of the serum geometric means to the air levels. For maintenance men, whose jobs involve all areas of the plant, the geometric mean of all area air samples for the individual plants was used. For maintenance apprentices and movemen, the area sample taken

TABLE 10.1. Serum PCB Levels of Various Worker Groups

		Group No	Aroclor 1242				Aroclor 1260				Net Accumulation Rate (ppb/yr) (Over Background)		
			GM ppb	In-Plant Service Yrs	N	Ratio to Background	GM ppb	In-Plant Service Yrs	N	Ratio to Background	Aro 1242	Aro 1260	
No Exposure (Non-plant control)			3	6.7	0	18	1.0	9.2	0	18	1.0	0	0
Employed, not Occup. Exposed*			4	50.4	23.6	18	7.5	11.3	23.6	18	1.0	1.85	0
Low Exposure*			1	179	16.3	102	25.7	26	16.6	86	2.6	10.6	0.96
•	Continuous at zone periphery		(L)										
•	Short, irregular high exposure		(M)										
Exposed Pop. Mean*			1	269	16.5	147	39.2	33	16.8	123	3.3	15.9	1.37
High Exposure*			1	676	17.0	45	101	59	17.4	57	5.9	39.4	[illegible].82
•	Continuous in exposure zone		(M)										

*Assumes continuous employment in exposed jobs

Employed since PCB Ban Works in treat area**	5	28.3	2	16	3.2	7.8	2	16	1.0	10.8	0

**Average area air level (1/78 - 12/80) = 57.3 $\mu g/m^3$

TABLE 10.2. Relation of Area Air Aroclor 1242 Levels to Serum 1242 Levels for Various Job Categories

	1979 Serum LPCB N	1979 Serum LPCB GM, ppb	1975 Area Air LPCB N	1975 Area Air LPCB GM μg/m³	Serum LPCB / Air LPCB
Large Capacitor					
Salvage & Repair	12	499	4	843	0.59
Filling	6	708	7	568	1.25
Maintenance	31	252	11	655	0.38
Small Capacitor					
Solder & Crimp	6	1176	4	850	1.38
Carrousel Oper.	9	447	9	813	0.55
Group Leaders	11	207	15	761	0.27
Salvage & Repair	3	191	2	569	0.34
Maintenance	12	417	15	761	0.55
Maint. Appr.	5	237	1	408	0.58
Movemen	3	175	1	408	0.43
QC & Test	23	314	2	569	0.55

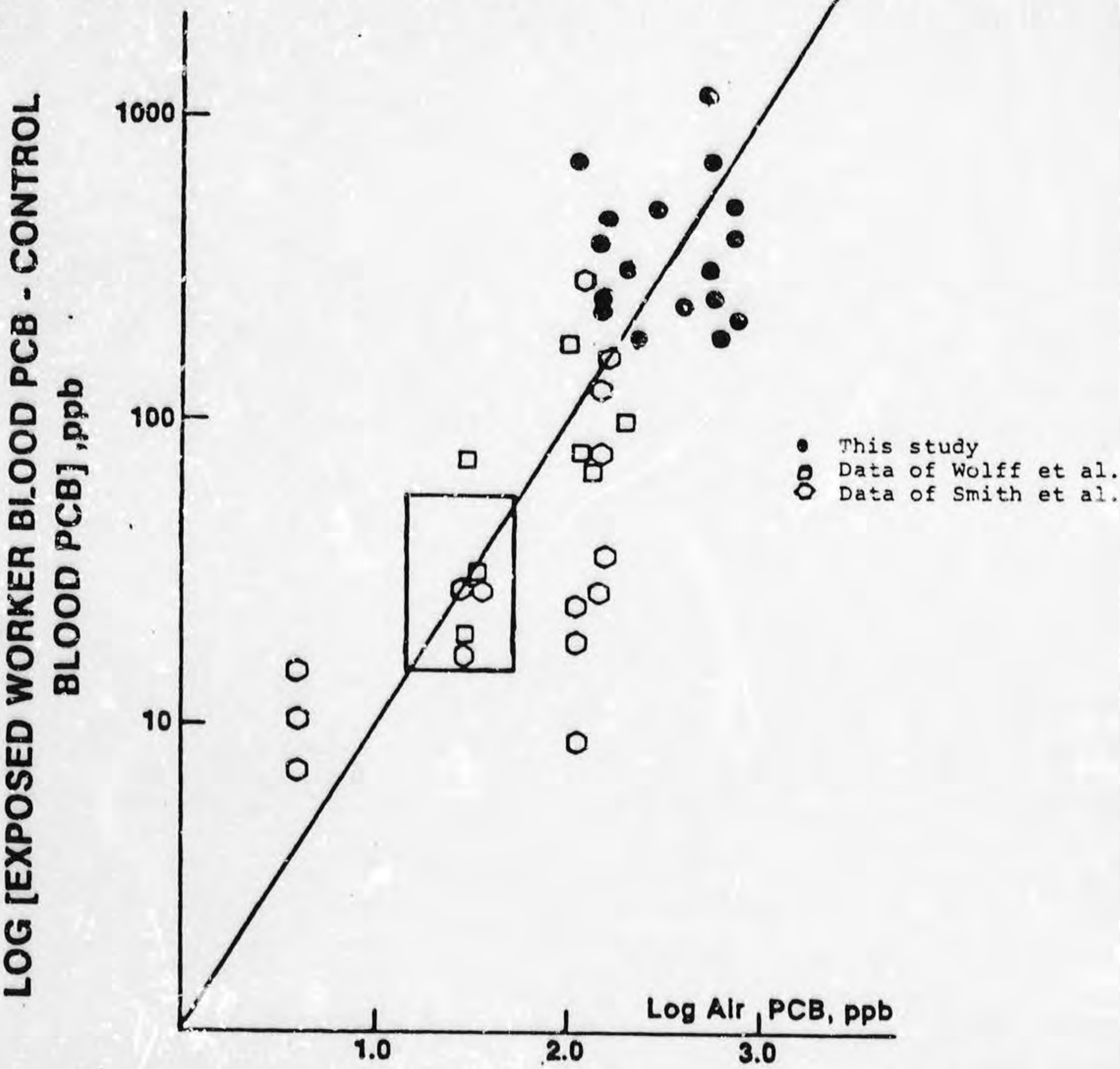
in the middle of the treatment area was used. The air values for salvage and repair and quality control and test were taken as the same.

Calculated total uptakes varied from 0.27 to 0.59 ppb per μg/m^3 in the area except for two job categories, large capacitor filling and soldering and crimping, where they were 1.25-1.38. If the average net uptakes for all other job categories (0.47 ppb per area μg/m^3) be considered primarily respiratory, the elevated uptakes in these two jobs can probably be related to dermal contact.

In Section 3 it was noted that personal air samples were approximately 50 percent of the area air values. This correlation suggests that for respiratory exposure the ratio of serum to personal air value is near 1 ppb/μg/m^3. In terms of net body burden this would translate to 4-6 mgms/μg/m^3 or (assuming the average exposure time to be roughly 10 years) about 0.5 mgm/μg/m^3/year.

In order to examine the generality and precision of this correlation, in Figure 10-1 we have plotted as solid circles the elevations in serum Aroclor 1242 above background for our directly exposed worker subpopulations; as squares, the corresponding elevations in serum L-PCB observed at the same plant by the Mt Sinai team (unpublished data kindly made available by M.S. Wolff); and as hexagons, those in L-PCB observed at a different plant by a NIOSH team (unpublished data from a draft report by A.B. Smith). In all cases, the air levels are given in terms of personal TWAs. The box

Figure 10-1. Increments over Background in Serum Aroclor 1242 as a Function of Personal PCB Air Level, for Three Capacitor Worker Groups.



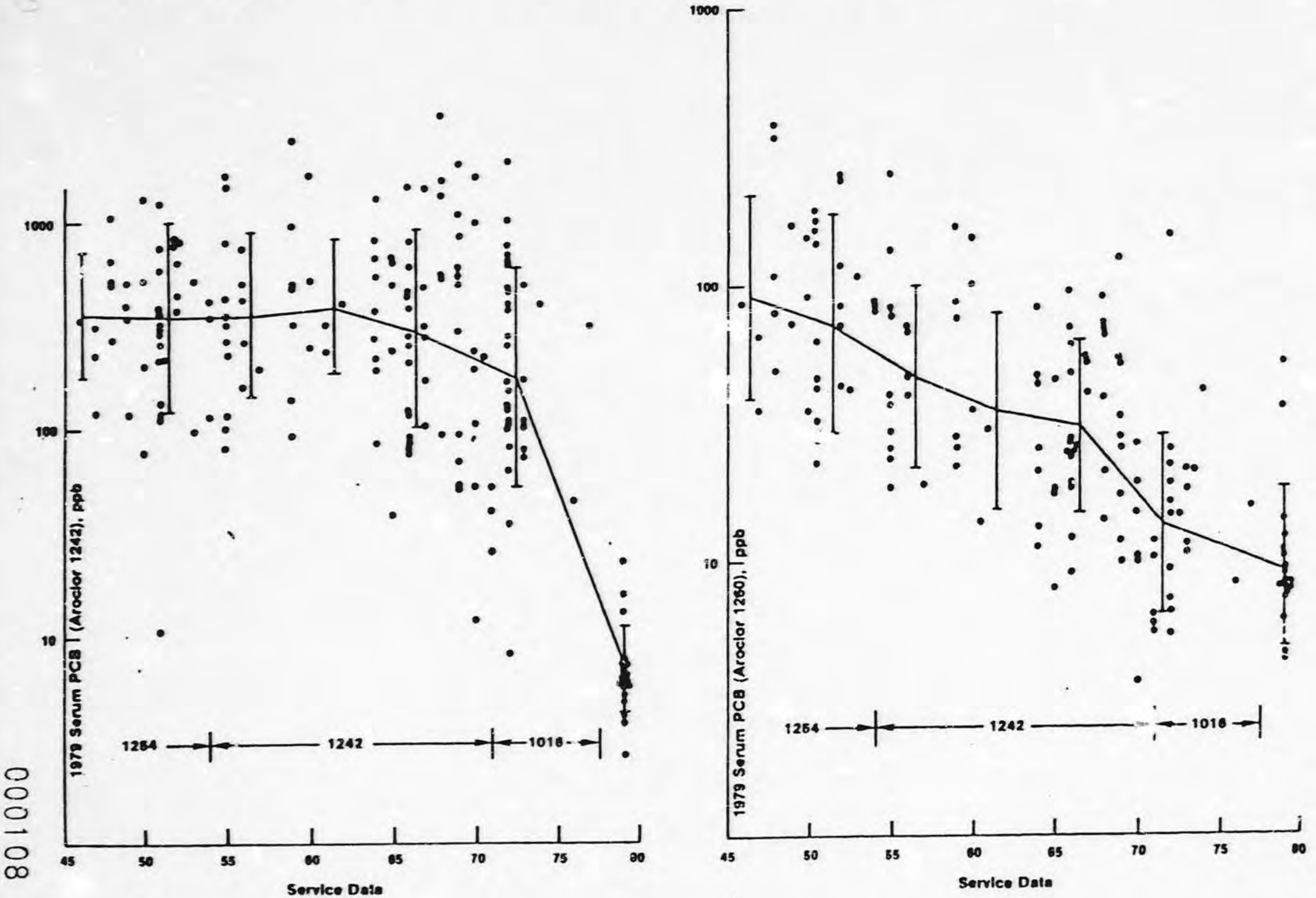
encloses the observations made in areas without direct occupational exposure.

It is seen that the data as a whole are distributed about a line of unit slope on the log-log plot, indicating simple proportionality between the variables, and that the mean ratio is indeed 1 ppb serum PCB increment for each $\mu g/m^3$ in the air breathed, or again roughly 0.5 $mg/\mu g/m^3/yr$. However, it should be noted that the scatter in the data shown in Figure 10-1 is sizeable, and that they do not provide clear evidence for dermal uptake.

In Smith's own examination of his data, he concluded that the dependence of log(serum L-PCB) upon log(air L-PCB) was much smaller than unity (as is apparent from the distribution of the hexagons shown in Figure 10-1), and that there was no correlation at all between log(air L-PCB) and log(serum H-PCB). The latter probably resulted from the low level of occupational exposure to H-PCB in his population in relation to the variance in the population background.

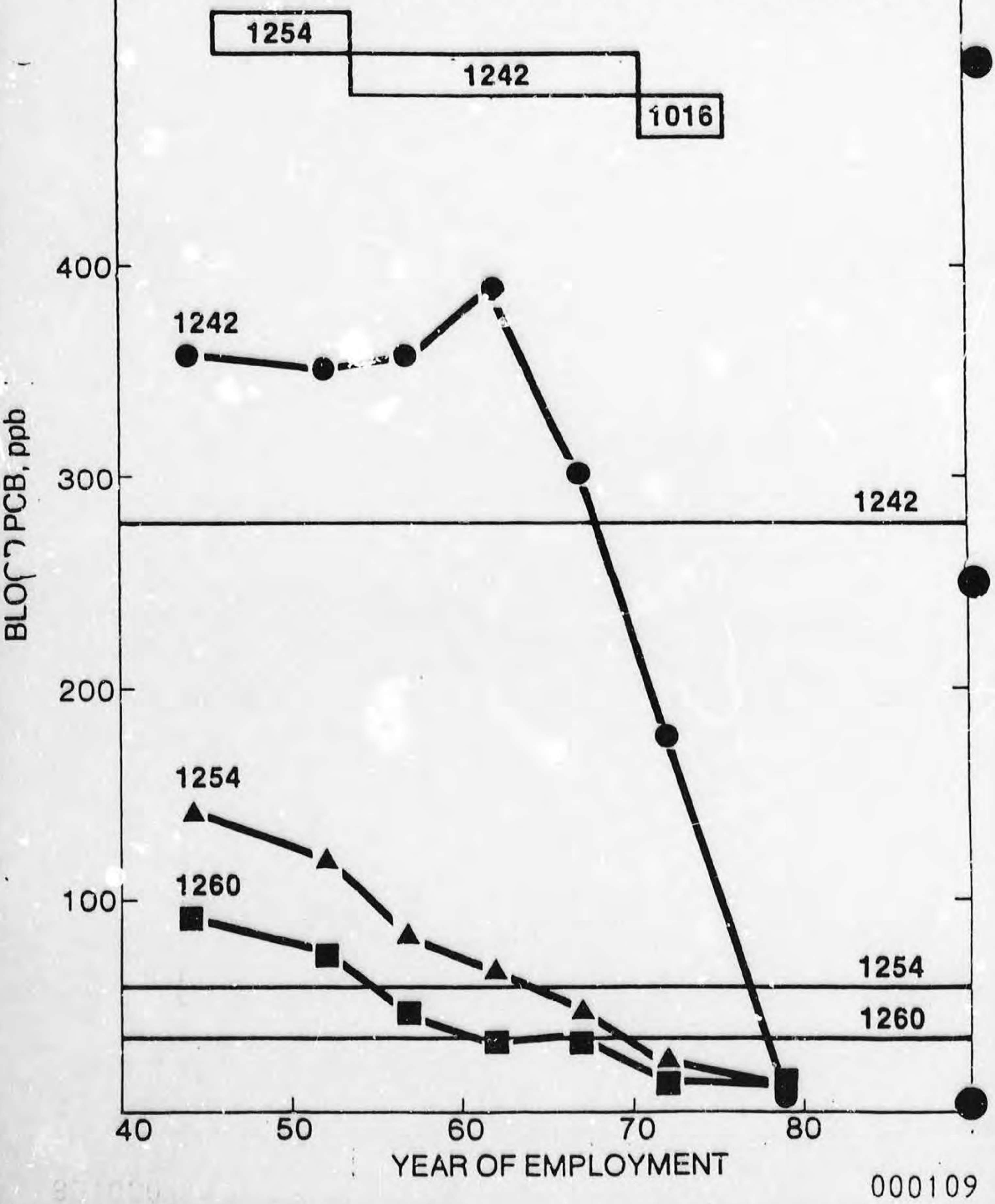
Turning from the mean intensity of exposure to the mean time of exposure as a contributor to PCB body burden, we show in Figure 10-2 the 1979 serum Aroclor 1242 and 1260 plotted semilogarithmically against service time for our entire study group. The Aroclor type and period of predominant use are shown between the arrows. The midpoints and termini of the vertical bars indicate the geometric means and standard deviations for 5-year groups. These 5-year geometric means are replotted in linear coordinates in Figure 10-3.

Figure 10-2. Dependences of Serum Aroclors 1242 and 1260 on Service Time for Directly-Exposed Capacitor Workers (Group 1). (semi-log plot)



000108

Figure 10-3. Dependences of Serum Aroclors 1242 and 1260 on Service Time for Directly-Exposed Capacitor Workers (Group 1) (linear plot).



It is apparent from Fig. 10-3 that the greatest rates of analytically reported "Aroclor 1254" or "Aroclor 1260" accumulation occurred back in the early 1950's, during the period of greatest Aroclor 1254 use, but that there was modest accumulation into the early 1970's, presumably arising from the presence of some species reportable as "Aroclor 1254" or "1260" in the Aroclor 1242 then in predominant use, and from the continued presence of Aroclor 1254 in the plant. Conversely, there was seemingly no increment in subsequently observed accumulation of "Aroclor 1242" resulting from exposure in the late 1950's, but an accumulation that increased almost linearly with time over the 1960-1977 period of Aroclor 1242 and 1016 use.

Discussion

Ideally, we should not be attempting to correlate serum PCB levels with either mean exposure levels or mean service time, but instead the total PCB body burdens with the sums of all time-exposure products. At present, we are attempting to use the exposure categories of Table 10-1 to categorize all jobs into three groups (indirect exposure only, low direct exposure and high direct exposure) and then to develop a time line for each individual detailing the number of months worked in each exposure category. Using the calculated uptake rates thus determined, a projected PCB level will be obtained and compared with the actual value found. In an initial study with three subjects the agreement between predicted and observed levels appeared poor, but work is continuing. At the moment, we are still not certain whether the considerable scatter in the uptake data arises because of our difficulties in quantifying the past exposures of our subjects, or because of individual variations in clearance rates, which would affect the observable net uptakes. A major reason for wishing to better quantify the cumulative update from job code history alone, is, of course, to permit better categorization of the exposures of the large numbers of mostly lightly exposed individuals involved in ongoing epidemiological studies of mortality, morbidity, and pregnancy outcome in the Hudson Falls - Ft. Edward employee population as a whole.

What the available data do show, however, is that for the population as a whole exposures to electrical grade PCBs can lead to net accumulations of higher PCBs and at least some isomers of the lower PCB's that can go on for many years. To a first approximation, the rates of accumulation are directly proportional to both the PCB level in the environment and the time of exposure, as would be expected. However, these rates are modest (ca. 0.5 mg per $\mu g/m^3$ in the air breathed per year), indicating that sizeable accumulations of environmental PCBs are not to be expected except in persons having prolonged direct exposure, such as the capacitor workers involved in the present investigation.

11. PCB Clearance

The present study has provided four observations from which order-of-magnitude estimates of PCB clearance rates in PCB-exposed capacitor workers may be made.

First, it is evident from Figure 10-3, that exposures to Aroclor 1254 that occurred 30 years before the time of measurement were still clearly recognizable as incremental contributions to the total levels of "Aroclor 1254" or "Aroclor 1260" measured in 1979. From this, it would appear that the clearance rate for the higher PCB homologs in this population must be <5% per year.

Second, Figure 10-3 also shows that those individuals first employed in the 1960's, during the period of Aroclor 124[illegible], exhibited levels of PCB measured as "Aroclor 1260" that were about 10% those reported as "Aroclor 1242," despite the facts that Aroclor 1242 itself contains only 5% of species reportable as "Aroclor 1260," and that additional exposure to Aroclor 1016, which contains no "Aroclor 1260" homologs, occurred in the 1970's. The simplest interpretation of this observation is that about half of the "Aroclor 1242" (as measured relative to 1260) had disappeared over the preceding 10-year period, meaning that, for those isomers used in determining "Aroclor 1242," the clearance rate was $\sim$5% per year greater than that for "Aroclor 1260."

Third, limited 1980 data on heavily exposed individuals (Group 2) who were included in the 1979 examination showed an average 1979-80 decline of 7% in those isomers used for reporting "Aroclor 1242."

This number is too far within the limits of experimental error to have much significance. (Use of comparisons between our 1976 and 1979 data to indicate clearance rates is precluded by the calibration error in the 1976 data for Aroclor 1254, and the continued exposure of the population to Aroclor 1016 during 1976-77.)

Fourth, the general appearance of the chromatograms, as noted in Section 7, was quite different in the L-PCB region from that of the Aroclor 1242 standard: most of the L-PCB peaks had either greatly diminished or disappeared completely. From this we may conclude that for some L-PCB isomers, the clearance rate may have been >100% per year.

More precise estimates of clearance rates for the various PCB isomers will not be possible until the 1979 chromatograms of the most recently employed persons have been examined on an isomer-by-isomer basis to determine disappearance rates of the more rapidly cleared isomers, and additional data is collected over the 1982-1990 period to quantitate changes in the more slower changing species. However, even the rough, order-of-magnitude estimates now available contrast sharply with some of those reported in the literature.

The best available data on lower PCB clearance rates in animals is that of Wood at Monsanto (1). Rats were fed diets containing 25 ppm of either Aroclor 1242 or 1016 for 30 days. During exposure and recovery periods sets of 5 rats were sacrificed and fat tissue samples were composited for each set. Fat was extracted and PCBs determined by peak area and reported as ppm on a lipid weight basis.

1
Wood, D. Chlorinated biphenyl dielectrics - their utility and potential substitutes. Nat. Conf. on PCB's, EPA-560/6-75-004, Chicago, Ill. Nov. 1975, pg. 317.

Figure 11-1 shows the results compared to those for a potential substitute (MCS 1238). We replotted data of the recovery periods from this Figure on semi-log paper and found them to exhibit the kinetic characteristics of simple, first order chemical reactions (Figure 11-2). This implies that all of the constituents of the Aroclor 1242 or 1016 were clearing from the rats at about the same rate, and that this rate could be characterized by a half-time of 22 days.

Returning from rat to human data, a follow-up study (2) on Japanese capacitor workers who had been exposed to Kanechlor 300 (a Japanese equivalent to Aroclor 1242, but which has also been reported to contain several ppm of PCDF) reported the half-time for clearance from those workers exposed less than 5 years to be only a few months, while that for workers exposed more than 10 years was 2-3 years. An obvious question is whether such "half-times" represented the times required for all of the PCB isomers to become half gone, or for half of the isomers to become gone completely. If the latter, this report would not be inconsistent with our findings.

The most striking - and most interesting - discrepancy is that presented by the clearance of the higher PCBs from victims of Yusho disease (poisoning with PCB-PCDF-PCQ mixture). Scattered early data on adipose tissue PCB levels suggest that a rapid decline in PCB levels occurred during the first year following ingestion; by 1973

2
Hara, I., A. Haruda, S. Kimura, T. Endo, and K. Kamano, Follow-up study of condensor factory after use of PCB discontinued. Jpn. J. Ind. Health, 1974, 10:365-6; 1975, 17:371-392.

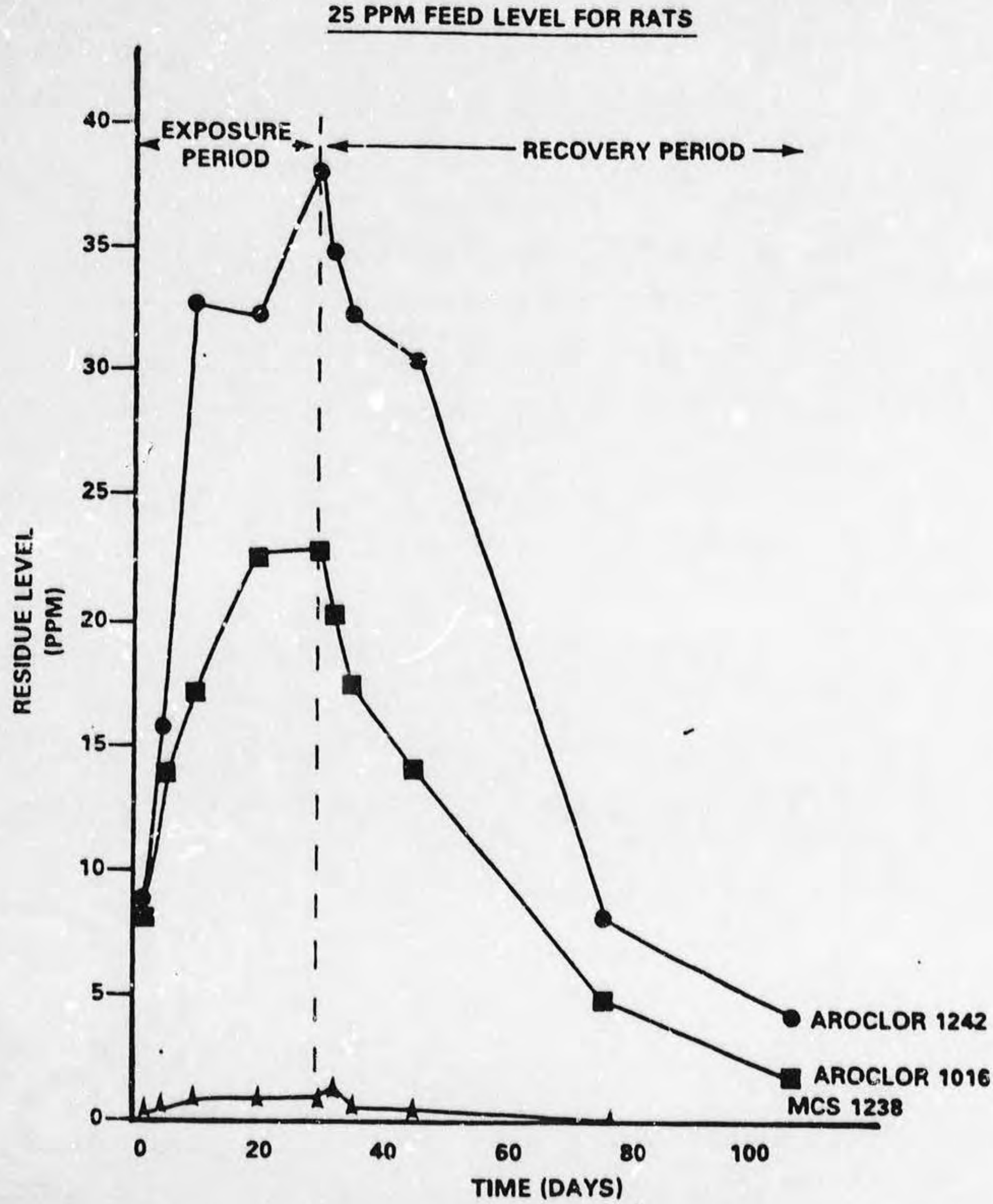


Figure 11-1 Results of rat tissue residue level studies vs. time, comparing Aroclor 1242, Aroclor 1016 and MCS 1238.

Figure 11-2

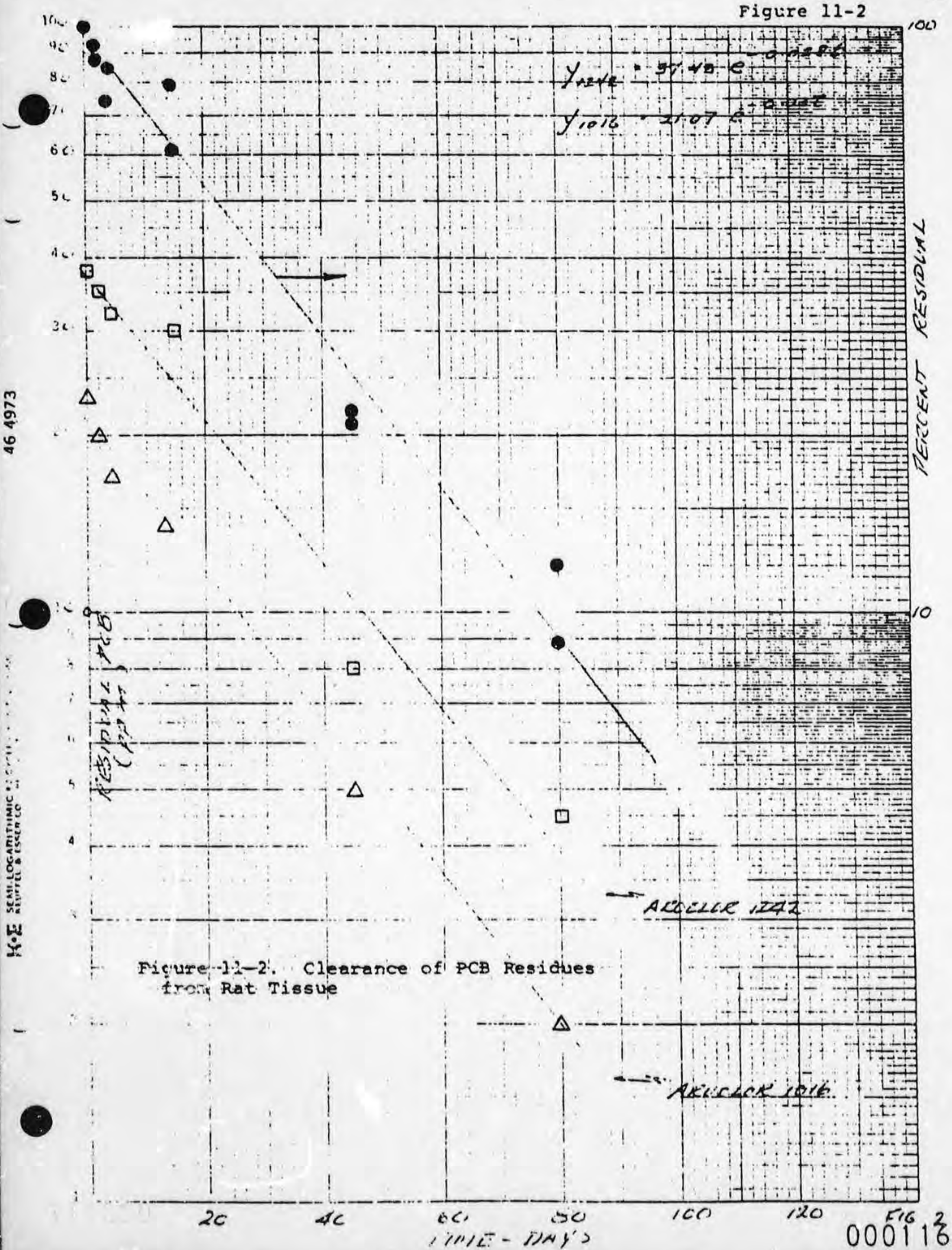


Figure 11-2. Clearance of PCB Residues from Rat Tissue

the blood PCB levels of the group as a whole were essentially back to Japanese background levels (3). A similar pattern appears to be emerging in the investigations of the 1980 episode in Taiwan (4). These observations imply a clearance rate constant for higher PCBs of 1-2 yr^{-1} for Yusho victims, in contrast to the $\sim$0.05 yr^{-1} for the comparable isomers in the Hudson Falls - Ft. Edward capacitor workers.

Our proposed explanation for this pattern of findings is that: (a) the PCBs themselves may induce P450 type mixed function oxidases in humans, as we have already noted; (b) the PCDFs, but not the PCBs are effective in inducing P448 type mixed function oxidases in humans, such induction being clinically manifested by chloracnecnic symptoms. (c) Many of the lower PCBs can be degraded by P450 oxidases; thus, since these lower PCBs can both induce P450s and be degraded by them, a ready mechanism exists for clearing such lower PCBs from exposed humans. (d) Many of the higher PCBs can be degraded by human P448 cytochromes, but not the P450s. Thus, since the PCBs do not readily induce P448s in the human, no effective mechanism will exist for oxidatively degrading the higher PCBs in an individual exposed to PCB alone. However, when a person is exposed to a PCB-PCDF mixture, induction of P448 will occur, and substantial PCB clearance will result. In short, the very slow clearance of PCBs in capacitor workers may be explicable on exactly the same basis as the

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3. Kuratsune, M., Y. Masuda, and J. Nagayama. Some of the Recent Findings Concerning Yusho. In: Proceedings of the National Conference on PCB's. November 19-21, 1975, Chicago, U.S. Environmental Protection Agency, EPA-560/6-75-004 (1976).

4. PCB Special Poisoning Issue, Clinical Medicine (Tapei) 7, No. 1 (1981).

absence of chloracne. This clearance pattern in ordinary, non-lactating adult humans apparently differs in several respects from that in the rat, where Aroclor 1254 is well known to induce both P448 and P450 oxidases, and where there is very rapid and complete clearance of all lower isomers, but where the higher PCBs can be fairly persistent, despite the demonstrable induction of P448. It also differs from that in the lactating woman, where it has been found that about half of all the PCBs present, higher and lower homologs alike, can be secreted in undegraded form in the milk about every six months (5). What all this suggests is that most of the capacitor workers' PCB body burdens are likely to remain with them the rest of their lives, as inert trace constituents of their fatty tissues, neither inducing harmful oxidase enzymes nor being affected by them.

5.
Yakushiji, T., Watanabe, I., Kuwabara, K., et al. Long-term studies of the excretion of polychlorinated biphenyls (PCB's) through mother's milk of an occupationally exposed worker. Arch. Environm. Contam. Toxicol. 7: 493-504, 1978.

12. Clinical Findings

A. Background

In 1975, prior to the present study, a review was conducted of current medical records covering a period of approximately five years. Employee census at the time was between 1500 and 1800. The following information was obtained on employees not occupationally exposed to PCBs.

1. One hundred and twenty-nine (129) employees had presented themselves one or more times with one or more of the symptoms of dizziness, nausea or headache from non-industrial causes such as viral gastroenteritis, nervous tension, inner ear problems, hypertension, infection, etc. (7.8%).

2. Twenty-six (26) employees had complaints of non-work related eye irritations or infections such as allergies, conjunctivitis, blepharitis, styes, etc. (1.6%).

3. Forty-eight (48) employees reported respiratory complaints or diagnoses which were not work-related such as cough, sinusitis, rhinitis, hay fever, asthma, bronchitis, pneumonia, etc. (2.9%). Two employees were removed from welding fumes because of the possibility of aggravation.

4. Seventy (70) employees presented with skin irritations or dermatitis (4.2%). Sixteen (16) of these were occupationally related to the following substances: paint, kerosene, flux, cutting oils, alcohol, acetone, Fuller's earth, oakite, Teflon

Delrin milling chips and weld flash. Fifty-four (54) were not related to the employee's work. They were diagnosed as fungal infection, eczema, insect bites, abscesses, drug reactions, nerves, scabies, athletes' foot, pityriasis rosea, chronic acne, psoriasis, impetigo and allergic reactions to cosmetics, detergents, leather, paint, poison ivy and other plants.

At the same time a review of the previous 15 years' medical records of individuals occupationally exposed to PCBS was conducted with particular attention to those removed from PCB work due to dermatological of other complaints.

1. Forty-nine (49) individuals presented with allergic contact dermatitis to PCBs or other constituents of the compounded dielectric fluid. This contact dermatitis cleared rapidly and usually without medication upon removal from exposure. One of us (J.F.), the plant physician, has never observed a case of chloracne in his 16 years of experience at the plants.

2. Sixteen (16) subjects were removed from PCB exposure in the 15-year period because of subjective symptoms such as nausea, dizziness, eye and nasal irritation and shortness of breath. Most of the employees had very short exposure (one day to 3-4 weeks). There were no physical findings and the symptomatology was attributed to odors and irritating fumes rather than specific toxic effects. Symptomatology cleared on removal.

B. Present Study

In the present study an history and physical examination was performed on 194 employees. In addition, laboratory data was obtained including chest x-ray, ECG, pulmonary function, an SMA-26 blood chemistry profile, hematology and urinalysis, as already described. The entire group was examined in 1976 and again in 1979. In the interim employees were seen on a rotating basis as a part of continuing medical surveillance program.

Physical examination was unremarkable in these employees and no signs of chloracne past or present was discovered. In particular, pigmentation and thickening of the skin, discoloration of the fingernails or enlargement of the Meibomian glands were not noted.

Data from the medical histories has not yet been examined in detail beyond simple tabulation. Findings are summarized for each employee in the Table appendices to this section.

1. Dermatological History

Seventy-five (75) employees (39 percent) had 100 dermatological findings in their medical history. These are tabulated in Table 12.1. The plethora of reports perhaps arises because of intense questioning in this particular area. Acne reports could be traced to its occurrence in adolescence and no active acne was reported.

Employees readily recognized the contact nature of most rashes (fiberglass, chemicals, dirty gloves, watch straps, soap, etc.). One subject had a rash related to the dielectric fluid. Two were clearly

TABLE 12.1. DERMATOLOGICAL HISTORY

Table 12.1. Dermatological conditions in the medical history of 194 PCB-exposed capacitor workers (Group 1). No cases of past or current chloracne were observed.

Rash	
Single episode	8
Pyranol 1	
Epoxy 2	
Intermittent	4
Contact	12
Neurodermatitis	4
Psoriasis	5
Dry, scaling, itching skin	8
Eczema	3
Hives	1
Seborrhea	
Dermatitis	2
Sebaceous cysts	10
Infections	
Boils	12
Abscess	2
Ringworm	1
Athletes foot	4
Eye Complaints	
"Granulating" eyelids	1
Dry skin	2
Tearing at night	1
Redness	1
"Growths," cysts (eyebrows)	2
Old Acne	4
Other	
Lipoma	4
Pilonidal cyst	2
Basal cell	2
Hemangiomia	1
Papilloma	1
Mole	1
Cyst, finger	1
Alopecia areata	1

related to epoxy exposure not related to dielectric fluid.

Many of the dermatological episodes antedated employment with the first episode occurring during military service. Because most employees have had multiple industrial exposures arising from job mobility, the nature of their work, e.g., as maintenance men or in the use of other chemicals such as solvents, it has been clearly difficult to relate these dermatological findings specifically to PCBS.

2. Gastrointestinal History

The findings from the gastrointestinal histories are summarized in Table 12.2. Data were reported as a physician's diagnosis, prior surgery or as complaints in 73 subjects.

Nine individuals reported episodes of jaundice, four of which occurred during childhood and three as prior to employment. One case during employment was related to gallstones. Four subjects reported five episodes of hepatitis only one of which, in a salaried staff employee, occurred during employment.

The incidence of cholecystectomy and food intolerance is presumably related to the elevated serum cholesterol levels observed in this population (Section 13). The incidence does not appear excessive (Figure 12.1). Although PCBS are detoxified by the liver and excreted in the bile, these data do not suggest serious hepatic or biliary dysfunction.

TABLE 12.2. GASTROINTESTINAL HISTORY

Table 12.2. Gastrointestinal conditions in the medical history of 194 PCB-exposed capacitor workers (Group I). One case of hepatitis occurred in a salaried staff employee; of the two cases of jaundice, one was related to gallstones.

	Male	Female	Total
Physician's Diagnosis			
Peptic Ulcer	7	3	10
Hiatus Hernia	7	2	9
Spastic Bowel	1	2	3
Diverticulitis	1	-	1
Intest. Obstruct.	-	1	1
Surgery			
Cholecystectomy	2	5	7
Hemorrhoids	2	1	3
Bowel Resection	-	1	1
Rectal Polyp	1	-	1
Complaints			
Food intolerance	6	1	7
Burning	3	1	4
Nervous Stomach	2	1	3
Flatulence	1	1	2
Vomiting	-	1	1
Unspecified	4	-	4
Jaundice			
Childhood	1	3	4
Pre-Employ.	2	1	3
Employ.	2	-	2
Hepatitis			
Pre-Employ.	2	1	3
Employ.	1	-	1

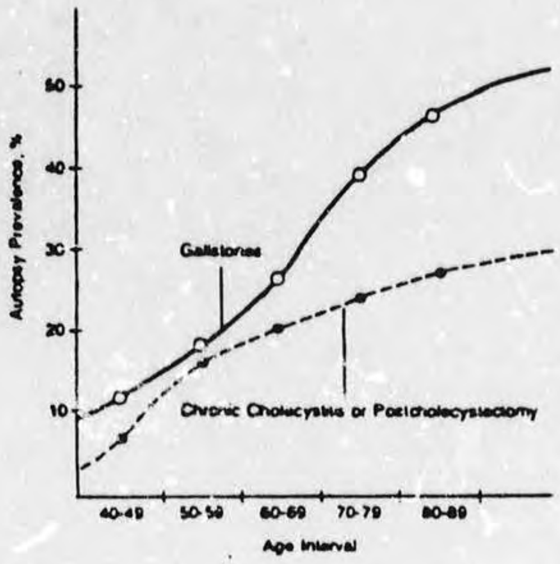

Figure 12.1. Autopsy prevalence of gallstones and gallbladder disease in Sweden. Gallbladder disease was documented as chronic cholecystitis or presumed to be present if a cholecystectomy was done. The greater prevalence of gallstones than gallbladder disease is consistent with the view that gallstone formation precedes the development of gallbladder disease. From Lindstrom (1977). Reproduced from Hofmann, A.F. Harvey Society Series 74, 1978, p. 26.

3. Neurological History

Fifty-four (54) employees mentioned one or more neurological complaints for a total of 73 such symptoms. These are contrasted with the complaints reported by Fischbein et al. in another study of employees at these plants (Table 12.3). In general, fewer such symptoms were mentioned by our highly exposed group compared to the Fischbein et al. volunteers. The most prominent complaints were headache and nervousness. Memory loss and somnolence were not reported.

Of those reporting neurological symptoms nine possible associated conditions were reported one or more times. The interrelations are shown in Table 12.4. For instance, of the 26 reports of headache, 6 individuals mentioned sinusitis, 3 mentioned hayfever or other allergy, 5 were heavy smokers with shortness of breath and morning cough, 1 woman was menopausal, 2 had hypertension under therapy, 1 has ASCVD, 5 reported their headaches as migraine, 1 employee had petit mal being treated by Dilantin and 9 subjects have or have had spastic colon or duodenal ulcer suggesting a broader psychosomatic basis for their complaint. In 7 cases such associated conditions were not mentioned. Of the total headache group four were or had been on tranquilizers.

The relations of Table 12.4 suggest that the reported symptomatology could be reasonably associated with intercurrent disease and/or life stress. The nineteen cases for which no associated condition was identified were generally stated as occasional occurrences and were not thought by the employee to be occupationally related.

TABLE 12.3. NEUROLOGICAL HISTORY

Table 12.3. Neurological conditions in the medical history of 194 PCB-exposed capacitor workers (Group 1). The date from the present study were compared to the findings of Warshaw et al. on a group of volunteer subjects at the same plants. Memory loss, fatigue and somnolence were not found.

	MALES				FEMALES			
	Mt. Sinai Volunteers (N=168)		Study Group 1 (N=153)		Mt. Sinai Volunteers (N=158)		Study Group 1 (N=41)	
	No.	%	No.	%	No.	%	No.	%
Headache	33	19.6	16	10.5	44	27.9	10	24.4
Dizziness	16	9.5	8	5.2	22	13.9	3	7.3
Depression	5	3.0	1	0.7	19	12.0	1	0.2
Memory loss	2	1.2	-	-	13	8.2	-	-
Fatigue	17	10.1	-	-	36	22.8	1	0.2
Nervousness	21	12.5	14	9.2	49	31.0	8	19.5
Sleeplessness	10	6.0	9	5.9	17	10.8	2	0.5
Somnolence	8	4.8	-	-	18	11.4	-	-

TABLE 12.4. RELATION OF NEUROLOGICAL COMPLAINTS AND ASSOCIATED CONDITIONS

Table 12.4. Relation of 73 neurological reports to 57 potentially associated conditions in 194 PCB-exposed capacitor workers (Group 1). Only 19 complaints, characterized as "occasional," were not related to this list of associations.

	No. of Neuro Complaints	Sinus-itis	Allergy	Heavy Smoking (SOB, cough)	Meno-pause	Hyper-tension	Vascular Insuffi-ciency	Migraine	Petit Mal	Psycho-somatic (spastic colon, ulcer)	No asso-ciation	Tran-quilizers	Total Asso-ciations
Reports of Assoc. Cond		11	4	6	2	3	2	5	1	13	10	19	57
Headache	26	6	3	5	1	2	1	5	1	9	7	4	33
Dizziness	11	5	2			1	1			3	1	3	12
Depression	1							1					1
Fatigue	2									2			2
Nervousness	22	4	3	4	1	4	1		1	5	7	12	23
Sleeplessness	11	1		2	1			2		3	4		9
	73	16	8	11	3	7	3	8	2	22	19	19	80

4. Other Symptomatology

In the cardiovascular area there were 25 individuals who reported a history of hypertension, most of whom had had therapy. Because of the reported association of serum PCB level with blood pressure, we have assembled the blood pressure readings made on our subjects but the analysis has not yet been performed. In our population three individuals have had myocardial infarctions and two others show evidence of ASCVD. There are four reports of rheumatic fever and one of erythema nodosum. There is one functional heart murmur. ECGs were consistent with these diagnoses or were normal.

There were 8 reports of kidney stones, one congenital kidney obstruction treated surgically and four reports of kidney infections. Five bladder infections were reported and one benign bladder tumor.

Respiratory symptomatology and chest x-ray findings are reported in relation to pulmonary function studies in Section 14.

DISCUSSION

In the study of Fischbein et al. there was no significant correlation between reported symptomatology and plasma PCB level or between reported symptoms and duration of employment. A statistically significant association was found between the L-PCB plasma levels and the dermatological findings on physical examination ($X^2 = 11.36$, d.f. 4, $p < 0.05$). The studies of Kreiss et al. did not address symptomatology.

1. Kreiss, K., Zack, M.M., Kimbrough, R.D., et al., Association of blood pressure and polychlorinated biphenyl levels. JAMA 245: 2505-2509, 1981.

Smith et al. have used logistic regression to model the relation between reported symptoms and serum PCB levels. The following symptom histories were significantly associated with either serum log (*L*-PCB) or log (H-PCB) or both, in the presence of confounders:

	log L-PCB $\sim \chi^{2*}$	log H-PCB $\sim \chi^{2*}$
Coughing on job or soon after work	5.05	3.87
Irritated or burning eyes	7.66	11.29
Unexplained loss of appetite	5.70	3.40
Unexplained tingling in the hands	5.16	3.51
Skin rash or dermatitis	0.04	4.51

$^*\Pr[\chi^2 \geq 3.84] = 0.05$

Maroni et al. reported 10 of 80 workers (13%) studied with acne and folliculitis of which three appeared to have active chloracne. They also reported five cases of dermatitis due to primary irritative or allergic sensitizing agents. In the three acne cases blood PCB concentrations were 310–495 ppb (mean 450 ppb) but did not differ significantly from the concentration of another five unaffected workers on the same job. All cases occurred in one plant using Piralene 3010 of French manufacture. The other plant with no chloracne used the Italian product, Apirolio. Both materials were 42 percent chlorine (equivalent to Aroclor 1242).

These investigators found hepatomegaly in 14 workers on physical examination. None had a history of excessive intake of alcohol or drugs. Eight of this group complained of symptoms related to digestive difficulties. Hepatomegaly was found in both plants. Although others have found biochemical changes (liver enzymes) associated with PCB levels in blood, this is the first report of liver findings on physical examination. Because of the subjective qualitative nature of the palpation of the liver edge we believe these findings should be regarded with caution. While alcohol consumption was described as ''not excessive,'' quantitative data would be helpful in comparing Italian to U.S. workers.

The symptomatology reported by workers is perhaps the least reliable of the data available for analysis. In the present study we have not yet performed a formal regression analysis. In view of the difficulties encountered by Smith et al. we suspect that the relations in the end will be tenuous. Accordingly, most of the effort of this study has been directed to the more objective biochemical and physiological measurements.

SECTION - Appendix. Medical history and complaints reported during clinical examination of Study Group #1.

ID#	Age	SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1001	53	None	None	None	None	1951-L. Kidney Surgery-Cong. Obstruction 1969-Surgery-Scar Tissue
1002	46	None	Headaches-None Since Quit Smoking-1970	Takes Valium for Nervousness - 5 mg. prn	None	1969-Surg. R. Kidney Stone Hiatus Hernia.
1003	23	None	None	None	None	Hemangioma 2"x4" L.Pectoral Inferior Axillary Area-Cong
1004	47	Fungus-Both Feet	Rectal Fissure	Migraine-2 yrs. Equagesic Tranquillizers	Slight Hay Fever	Hiatus Hernia 1975-Septoplasty Elec. Burns, Scalp - Plastic Surgery
2005	39	None	Diarrhea - Spastic Bowel	Dizziness - DM (Prior to Dx.) Valium, prn Insomnia - Assoc. Fatigue & Nervous	None	Diabetes Mellitus Jaundice - Age 5 1964-Rem. Benign Polyp - Vocal Cord 1973-Manchester Repair
1006	38	None	Indigestion - Relates to Greasy Foods	Insomnia-Recent	S.O.B. - Relates to Smoking	Achilles Tendon Repair-1969
1007	37	Neurodermatitis Since Service 1962-1966	None	None	None	None
1008	44	Rash-Palm R.Hand Superficial Skin Peeling-Comes & Goes	Ulcer-1976	None	None	1945-Appendectomy Arthritis - Knees 1975-Rem. L. Patella 1973-Kidney Stones
1009	33	None	None	None	None	None
1010	45	3 Times in 9 yrs. Clears Spontaneous.	Indigestion - Coffee-Fried Eggs	None	Sinus	1956-Pilonidal Cyst Acne Pits on Face
1011	44	None	Ulcer-Healed	Hypertension - Librium.	None	Hypertension 1974-L. Kidney Stone 1960-R. Inguinal Hernia
2012	55	None	None	None	None	1964-Acute L. Pyelitis 1970-Fibroid

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COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	N...ROLOGIC	RESPIRATORY	OTHER
1013	53	None	None	None	None	1932-Appendectomy 1973-Rem. Benign Bladder Tumor
2014	62	Hx. Psoriasis "Years Ago"	None	None	None	1951-Bartholin Cyst
1015	47	None	None	Dizziness	P.N. Drip-Year Round Allergy Shots - 3 Years	1956-L. Inguinal Hernia
1016	45	None	None	None	Probable Emphysema - CXR	1975-Bladder Infection 1973-R. Inguinal Hernia 1968-Pyorrhea
1017	42	Eye Lid Cysts-Rem. by Burning. Hx. Rash 1973 - Cleared w/Treatment	None	None	Emphysema - CXR	None
1018	29	None	None	None	None	1970-Fx. L. Ribs, Facial Laceration-Auto Accident
1019	64	None	None	None	None	Dorsal Osteoarthritis
1020	39	None	None	Insomnia, Occ.	None	1974-R. Pituitary Tumor Hiatus Hernia Obesity
1021	39	None	None	None	P.N. Drip - Chronic Sinus	Frequent Indigestion - In Service
1022	30	Lg. Pimples-1971	None	1972-Headaches-Nervousness-No Rx.	Hay Fever-Pollens	1970-Appendectomy Fatty Tumor off L. Arm as Teenager
2023	53	Neurodermatitis Dr. Wells-1948-Every 4-5 years.	None	None	Frequent Colds-Stopped Smoking 4 Mos. Ago	1937-Appendectomy
1024	26	None	None	None	None	1965-Ruptured R. Ear Drum
1025	26	None	Recurrent Indigestion w/relief from food - ? Ulcer	None	None	None

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
2026	48	Occ. "Itches" Assoc, w/Nerves Acute Psoriasis-1965	None	None	None	Appendectomy - Child 1950-Plastic Rem. Burn Scar-Arm 1974-D&C & Rem. Bilateral Tubo-Ovarian Mass
1027	62	None	Peptic Ulcer-Healed Vomited w/Ulcer	Headaches-Datril Nervousness-Liberax Occ. Insomnia	S.O.B. After Flight of Stairs Smokes 1.5 packs for 30 years	1967-Healed Peptic Ulcer Hiatus Hernia 1971-Hemorrhoidectomy
1028	31	None	None	None	None	1969-Surgery Knee
1029	27	None	Frequent Indi-gestion (Ulcer)	Insomnia - Takes Nytol	None	1975-Healed Ulcer
1030	51	None	None	None	None	1974-Hypertension 1953-Hepatitis
1031	22	None	None	None	None	None
1032	46	None	None	None	None	M.I. - 1968 Hiatus Hernia
1033	49	Occ. Arms & Legs itching (Skin Dry, Scaley)	None	None	None	Hypertension
1034	35	None	None	Dizziness assoc. w/ TCE Exposure	Sinusitis	Sinusitis w/Septal Defect
1035	43	Psoriasis - Hands, Elbows	Rectal Fissure	None	Hay Fever-Allergic to Cats, Grass, Ragweed, Sinusitis	1973-Bladder Infection
1036	45	Skin Rash - Fiberglass React,	None	None	None	None
1037	36	Dry Skin - Winter Months	None	Dizziness - When not Wearing Glasses	None	None
1038	37	Athlete's Foot	None	None	None	Has benign, functional Heart Murmur
1039	36	None	None	None	None	None
1040	43	None	Nervous Stomach	None	None	1946-Jaundice 1965-L. Disc Removed 1974-GI Series-Normal

COM[ ]LAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
2041	57	Old Acne & Pigmentation of Face - Since Age 20	None	Hot Flashes - Menopause	Is Hoarse at Times - Sinusitis Years Ago	Appendectomy - Age 18 Rheumatoid Fever - Age 26 Eyes - Allergic to Soap & Hair Spray 1966-Hysterectomy
1042	58	None	Assoc. w/Duodenal Ulcer, 3 yrs. ago	None	None	Post Prandial Glucose-134 Hypertension Prostatitis-15 years
1043	25	None	None	None	None	None
2044	57	None	None	None	None	1951-RF Arthritis, Arms, Legs 1967-Hypothyroidism
1045	39	Boils - Sebaceous Cyst - Back	None	None	Sinusitis - Occ. S.O.B. - Smokes 2 Packs Daily	1966-Kidney Stone (? Side) 1968-Ringworm
2046	49	None	Occ. Indigestion - Food	None	None	Hiatus Hernia
1047	41	None	None	Dizziness - Nerves -Valium, tid	Chronic Sinusitis	Hiatus Hernia Skin Grafts - Lower Legs
1048	52	None	None	None	None	Jaundice - Age 8
1049	52	None	None	Dizziness - Takes Pavabid: Headaches relieved since on Pavabid	Sinus & Colds	Acne as Teenager Skin Cyst Rem. From L. Temple TB in 3rd Grade
1050	24	None	None	None	None	None
2051	43	Occ. Itching w/Dry Skin - No Rash	None	None	None	1975-Fatty Cyst L. Arm 1957-Ovarian Cyst R. Side
1052	49	None	None	Occ. Insomnia	None	None
1053	62	None	None	None	None	M.I.-1975 (Ant. Lat. Wall) Hypertension
1054	27	Chronic Der[mat]itis Nerves-10 Years	None	None	None	Chronic Eczema Hands & Fee[t]
1055	30	None	None	None	CXR-Possible Emphysema -Smokes 1 Pack Daily	None

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1056	32	Seborrheic Eruption -Chest- Clears in Summer	None	None	None	Recurrent Sub Acute Ch. Seborrheic Eruption Since Service 1965
1057	52	None	None	Headaches-Vision- Assoc. w/Vascular Insufficiency	Smokers Cough	Vascular Insufficiency , 1967-Indigestion-Now Normal
2058	43	None	None	None	None	None
1059	30	None	None	None	None	None
1060	25	None	None	None	CXR-Long Standing Chronic Pulmonary Infection	(PF Normal) ? Healed TBC or Healed Histoplasmosis
1061	42	None	Intolerance to Fried Food, Coffee	Migraines Since Age 10; Anxious, Depression; Occ. Insomnia	None	Takes Thyroid gr.II for 2yrs 1976-Kidney Gravel Hypertension-No Medication Pounding Heart w/Nerves 1947-Abscesses both Buttocks Allergy to Penicillin
1062	28	None	Indigestion - Hiatus Hernia	None	None	Hiatus Hernia
1063	38	None	Stomach Pain - Nerves	None	None	None
1064	30	None	None	None	Occ. Nasal Stuffiness	1970-Jaundice Assoc. with Gall Bladder Stones
1065	46	None	None	None	None	History of Rash - 6 or 7 Years Ago 1974-Vasectomy
1066	46	None	None	None	None	None
1067	24	None	None	None	None	Hypertension-No Medication (140/90)
2068	49	None	None	Occ. Headache	Occ. Stuffiness	None
1069	37	None	1971-Burning Sensation in Stomach	Headaches (Tension for past 3 years) Nerves	Pulmonary Emphysema Heavy Smoker Since Age 16	1971-Hyperthyroid 1968-Rash on Both Arms for 3 to 4 days

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COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1070	59	None	None	None	Coin Lesion-[illegible] (Smokes 2 p[illegible] daily for 40 [illegible])	1971or1972-Inf. Sebaceous Cyst-R. Neck
2071	53	None	Spastic Colon-Colitis-7 yrs.	Claims Nerves & Headaches Since Elec. Shock-1974	None	Arthritis-Spine, Fingers 1972-Thyroidectomy 1963-Hysterectomy
1072	34	Occ. Itching on Arms-dirt, dust, Some Chemicals - 24-48 hrs.-Treated only by Skin Washing After Exposure	None	None	None	1967-Abdominal Injury - Auto Accident - Torn Intestine
2073	46	Skin Rash-1975 - Related to "Dirty Gloves" - No Recurr.	V & D about once a Month-GI Upset	Dizziness Assoc. w/Tachycardia(PAT) Nervous-Valium	None	Swelling of Eye Lids in AM History of Kidney Infection Years Ago 1974-Rem. Benign Cyst of Breast and Back 1954-Partial Hysterectomy Menopause
2074	45	None	"Nervous Stomach"	Sinus Headaches - Winter	None	Ch. Kidney Infection 1966-Rhinoplasty
1075	31	None	None	None	None	None
1076	38	Claims 1968 Rash Tips of Fingers-Not Seen - Rash Under Watch Strap	None	None	None	None
1077	49	None	None	None	None	None
1078	28	Boils-7-8 yrs.ago Cyst of Neck - 8 yrs. ago	None	None	Frequent Colds & Sore Throats past 3 yrs.	1974-Slight Hypertension R.F. - Age 12
2079	57	None	None	Migraine Headaches Insomnia-Menopause	None	Appendicitis-Age 22 Tubal Ligation-Age 27 1966-Hemorrhoidectomy
2080	60	None	None	None	Poor P.F.-Dentures	1935-Appendectomy 1965-Cholecystectomy 1952-Fibroids, Hysterectomy
1081	[illegible]	Boils-(All my Life)	None	Nervous-1 Mo. Ago T[illegible] "Mild" Nerve P[illegible] 12/75	None	1975-Prostate Infection

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1082	56	Mild Psoriasis L. Elbow & Knees	Freq. Indigestion Takes Rolaids	None	None	1964-Cholescystectomy 1961-Kidney Stone 1975-Prostatitis
1083	24	None	None	None	None	None
1084	31	Athlete's Foot	None	None	None	Polio - Age 4 P.F.
1085	50	None	[illegible]	Occ. Insomnia	None	1972-Hemorrhoidectomy
2086	55	None	None	None	None	1968-Thyroidectomy 1968, 1972-Benign Cysts from Breasts
2087	58	None	Ulcer-1973; Intestinal Obstruction-1971 & 1975 Ulcer-1975	None	History Emphysema about 1973 History Pneumonia, Chronic Bronchitis	General Debilitation 1970-Hysterectomy 1971-Temp. Colostomy - Bowel Obstruction 1971-Rem. Portion of Large Intestine 1973-Cholecystectomy
1088	55	? Sclerodermatitis (Rash Comes & Goes for Years)	None	None	None	P.F. - Low - Has Small, Thin Chest-Heavy Smoker.
1089	41	1972-Boil, Arm & Rectal Area	None	None	Sinusitis-Allergic to Cats, Dust, Potatoes	1972-Rem. Sebaceous Cyst on L. Neck, Chin
1090	30	1967-1968-Boils in Service - R. Buttock and Face	Indigestion 3-4 Times Monthly	None	Some stuffiness "When Fatigued"	1968-Intestinal Blockage from "Nerves" - After-Discharge from Service
1091	37	None	Indigestion - Assoc. w/Food	None	Sinusitis; Some S.O.B.-Mostly Summer; Fx. Nose 1966	None
1092	42	None	1968-Bleeding Ulcer	None	None	None
1093	64	None	None	None	None	None
1094	36	None	None	None	None	None

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1095	32	1964-Reacted to Chlorine in Service	None	1974-Nervous Took Tranquill-izers	None	None
1096	66	None	None	None	CXR-Calcified Granuloma-RUL	Hypertension-On Medication CXR Reveals Slight Cardiomegaly
1097	25	Had Cyst Rem. from Bridge of Nose	None	None	None	None
1098	54	None	None	None	None	R. Lung Drained-Age 5 or 6
1099	30	None	None	None	"Blows Nose" Freq. Throughout Year	Appendectomy - Age 12
1100	54	Boils in Service-Had Shots for Them-NO Problem Since; Benign Papillomata Upper Chest & Low Middle Back	None	None	None	Redness of Eyes Since Childhood Hypertension-On Medication
1101	26	1972-Boils None Since	None	None	None	Poor Effort on P.F. CXR-Normal
2102	29	None	Indigestion - Hiatus Hernia	Petit Mal - On Medication Age 9-16 "Sinus" Headaches	None	Hiatus Hernia Ptosis - Left Kidney 1971-Del. Normal F. Infant
1103	46	Boils-As Teenager None Since Dry Skin	Intolerance to Spicy Foods	None	None	None
2104	36	None	None	None	None	5 Pregnancies - One during Employment (Normal)
2105	60	States Had Itching in 1960 while in QC-No rash to PCBs	None	None	Occ. Sinus Problem Takes Dristan	1951-Hysterectomy 1955-Rem. Laryngeal Plaque Ptosis of Right Kidney 1973-Bronchopneumonia Miscarriage Prior to Emplo 1941-7 Month Normal Del-A&W

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1106	42	None	None	None	None	None
1107	41	None	"Heart Burn" Gas	None	None	"Feels" B/P Elevated When Excited (Dropped out of Study)
1109	54	None	Indigestion - Assoc. w/Alcohol & Certain Foods- Takes Pathibamate Has Diverticulitis	None	None	None
1110	27	None	None	None	None	None
1111	44	None	None	None	None	None
1112	30	None	Diagnosed as Ulcer 11/75 (No X-Ray)	None	None	1971-Encephalitis in Servi 1/76-On Gantrasin for Cystitis-Prostatitis
1113	50	None	None	None	None	None
1114	29	None	Occ. Indigestion- Relieved by Rolaids "Spastic Bowel" - Treated at ER 12/75	Rare Dizziness Assoc. w/Headaches Occ. Has Brief Sharp Head Pain Lasting 5-10 Sec.	None	1975-Normal Lower GI Serie 1954-Left Foot Drop following Auto Accident
2115	25	Rash 1973 - No Reoccurrance - ?Relationship to PCB	None	None	None	2 Pregnancies Prior to Employment -None Since
2116	60	None	None	None	None	1958-Cholecystectomy Hypertension-No Medicatio
1117	57	1970-"Growths on Eyebrows"	None	None	None	1972-Cholecystectomy
1118	47	None	None	None	None	Hypertension 1973-Auto Accident - Contused Spleen, Repair o Intestine
1119	29	Had Rash 1 Week - 1976-Cleared-Rem. from Pyranol	None	None	None	None

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1120	22	Has Small Inactive Branchial Cleft Cysts Behind Both Ears	None	States He "Shakes" All the Time Since Childhood	None	None
1121	25	Had Rash When First Assigned To Film Area - No Irritants	None	Headaches Prior To Nasal Surgery 1973	Has Frequent Runny Nose	1964 or 65-Kidney Infectio
2122	35	Alopecia Areota - Dx. by Dermatologist as Caused By Nerves - First Episode Age 13	Occ. Heart Burn i.e. Orange Juice	None	Occ. Feels She Isn't Taking In Enough Air	1972-Acute Arthritis - Erythema Nodosum 1966-Benign Fatty Tumor Rem. from Left Breast & Left Shoulder 2 Normal Pregnancies - Non Since Employ. by Choice - B.C. Pills & Rhythm
1123	33	Chronic Dry Skin - Cracking of Fingertips	None	Took Medication For Nerves Up to About 8 Mo. Ago	Heavy Smoker - Coughs & Raises Every AM	None
2124	43	None	None	Under Psychiatric Care-Mellaril 200 mg. - Has Not Had Usual Headaches Lately	None	Had Shots For Hay Fever
1125	49	Hx. Boils 15 Yrs. Ago	Occ. Indigestion-Peptic Ulcer 20 Yrs. Ago	Migraine Headache Last Year Occ. Insomnia	Heavy Smoker - Coughs & Raises Every AM Occ. Sinusitis	None
1126	58	None	Indigestion - Rolaids	Rare Dizziness - (Hypertension)	None	1970-Myocardial Infarctio
1127	32	None	None	None	"Strep Throat" Freq. - Takes Penicillin Constantly	Poly-Arthritis 1973- R.F.
1129	52	None	None	None	None	1968-Pilondial Cyst

0000141

000142

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
2128	52	Had "Rash" 1969 (Non-Ind. Rash on 5th Finger Aggrav. by Heat of Soldering Iron - Rem. from Sealing)	None	None	None	Treatment For Hypertension For 4-5 Years Pyorrhea 4 Normal Pregnancies - 1 Full Term Stillborn. (1 NFTD During Pregnancy) 1972-Hysterectomy
1130	26	None	None	None	None	1975-Rem. Bilateral Varicocele
1131	24	None	None	None	None	1968-R. Hydrocele
1132	47	Boils, Acne As Teenager	None	In Past, Took Valium for Nerves None Now	Sinusitis Treated Twice by ENT Spec. in 4-5 Years	1956 (About) Passed Kidney Stone 1963-Hemorrhoidectomy
1133	49	None	None	Occ. Headaches	S.O.B. - Rib Cage Arthritis - Poor Expansion	Since 1962- Has Severe Arthritis - Generalized
1134	30	Boils As Teenager	None	None	Sinusitis as Child	None
2135	39	None	None	None	None	None
2136	45	Itches to Some Soaps	None	Takes Medication For Nerves	None	Had Jaundice as Child 1974-Took Thyroid 1974-Hysterectomy - CA of Cervix No Pregnancies During Empl 3 Normal Preg. - 1 Died at 6 Days (Premature) 1974-Benign Tumor of Breast
1137	48	None	"Possible" Hiatus Hernia	Nervous-Takes Valium - Post Coronary Insuff.	Occ. S.O.B. w/ exertion, Mild Occ. Sinus Complaint	ASCVD 1967-Acute Coronary Insuff. 1973-Rem. of Cyst-Ring Finger
2138	41	None	None	None	None	Hepatitis Twice (Last Time 1966) Several Kidney Infections No Pregnancies-Deliberate-Separated

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
2139	28	Breaks Out in "Hives" from Chocolate	None	None	None	2 Normal FT Deliveries during Employment
2140	49	Athlete's Foot	Has "A Lot Of Gas"	Occ. Gets "Light Headed" Nervous-Treated in 1970	None	Hypertension- Under Treatment
2141	27	None	None	None	"Cigarette Cough" S.O.B. Climbing Stairs-Heavy Smoker	1948-Twins - NFT 1959-NFT Delivery During Employment 1968-CA of Cervix
2142	31	None	None	None	None	1970 - Jaundice 1 Week X-ray for G.B. Attack-Neg. 2 Normal Pregnancies Prior to Employment - None Since
1143	56	Psoriasis-R. Leg Dry Skin Athlete's Foot	None	"Nervous"	Heavy Smoker - S.O.B.; Sinus	Petit Mal-Dilantin Hypertension
1144	29	None	None	None	None	1974-Excised Cyst-L. Check
1145	27	Low Grade Granulating Eyelids	None	None	Sub-Acute Sinus Since Teenager-Year Round - P.N. Drip - DX. in Serv.	Refused Chest X-ray
1146	52	None	None	None	Allergic to Dust	None
1147	53	About 3 Yrs Ago-Rash-Blister Like-Treated by Dr. Little (not assoc. w/PCB)	Occ. Heartburn	Frequent Headaches in Past Year	None	1963-Rem. Benign Rectal Polyp
1148	59	Dry Skin-Works in Lab-Freq. Hand Washing, Uses Acetone	None	None	None	1974-[illegible]tectomy 1973-Ce[illegible] Fusion 1969-Cervi[illegible] Disc Removed

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1149	51	None	Since 8 Mo. Ago-Small Amt. Bright Rectal Spotting	Occ. Dizziness	None	None
1150	60	1975-Left Leg Skin Rash	None	None	None	1944-Jaundice (In Service) 1971-Urinary Infection
2151	54	None	1971-Duodenal Ulcer (Healed)	Headaches w/ Fatigue-Relieved w/ASA & Rest	None	1948-Hysterectomy (Prior to Employment) Had Asthma with Allergic Reaction to Penicillin
1152	28	None	None	None	None	1973-Infected Prostate
2153	49	None	1963-Peptic Ulcer (Healed)	None	None	R. Inguinal Hernia-Age 14 1971-Excision Benign Tumor Left Breast 1968-Rem. of Irritated moles 1970-Rem. Skin Cancer(Back)
1155	43	None	Indigestion - Corn & Spaghetti	Dull Headaches-Lasts 8-9 Hrs. 4-5 Times Weekly	Has Sinus Problem upon Arising & In Evening	Eyes Tear at Night (Not at Work) 1975-(Spring) Hypertension (12/75-B/P 148/92) 1967-Fatty Cysts Rem. from Chest & Back
1156	33	None	None	None	None	1971-Infectious Hepatitis 1968 or 1969 - V.D. 1975-Abdominal Gun Shot Wounds
1157	28	None	None	None	None	Appendectomy - Age 10 Burn Scars Medial Calf
2158	58	Skin Itching w/Nervousness-No Rash	None	Nervous-2 Mo. Ago Took Medication	None	1975-Cholecystectomy Hypertension - Mild 1969-Benign Tumor Rem. Right Breast
1159	50	Occ. Skin Rash-Buttocks, Anal Area, Penis (No Rash 1/76)	Indigestion about 4 Yrs. Ago with Tension	Had Nervous Prob. 4 Yrs. Ago - No Medication Now	None	Hypertension with Nerves

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
2170	61	None	Hiatus Hernia	Occ. Headache; Nervous-On Tranquillizers	None	1974-6 Mo. ASCVHD 1968-Hysterectomy Bilateral Herniorrhaphy
1171	31	Allergic To Wool, Eczema 10 Yrs. Ago	None	None	None	None
1172	24	None	None	Was Discharged From Service due to "Nervousness"	Sinus-Hay Fever	None
1173	28	Comp. of Dry Skin Around Eyes At Times When Working w/ PCB's-None Seen	None	None	None	None

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
2160	56	None	None	None	None	1971-Hysterectomy due to Fibroids 1966-Had Skin Reaction to Epoxy - Temporary Removal
1161	26	"1 Yr. Ago - Skin Rash" (? Cause) - "Very Minor"	None	None	None	1975-Abscess Left Cheek
1162	36	None	None	Occ. Insomnia	None	None
1163	41	None	None	"Tension" Headaches	None	None
1164	34	None	None	"Tension" Headaches	Hay Fever to Dust-Frequent Colds (2 Pk. Day-Smoker)	None
2165	32	Occ. Skin Itching Assoc. w/Allergies	None	Migraine-Assoc. w/Menses. Occ. Dizziness at Work On Valium for Nerves	Sinusitis-Assoc. w/Allergies (Dust, Oranges, Pollens)	None
1166	29	None	None	None	Sinusitis (Light Smoker)	None
2167	37	Has Rare Eczema During Winter Mos.	None	None	None	2 Miscarriages - 1963-at 4 1/2 Mos. (Prior to Employment) 1969-at 2 Mos. (No PCB Exposure) 5 Normal Deliveries
2168	46	Had Temporary Rem. for Epoxy Rash-No Rash Since	None	None	None	1968-Cholecystectomy 1975-Vein Ligation Jaundice-Age 12
1169	54	None	None	Takes Valium For Nerves (Palpitation Sweats)	S.O.B., Sinus Headaches, Smokes for 35 Yrs. (1 Pk. Daily)	Hypertension for 2 Yrs. Polio - Age 23 V.D. - 35 Yrs. Ago

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1174	50	None	None	None	None	Hypertension 1944-Scarlet Fever 1960-Hemorrhoidectomy
1175	44	None	Occ. Heartburn Hiatus Hernia	None	Has PN Drip	1975-Took Medication for Several Months for Hypertension 1970-Vasectomy
1176	51	None	None	Headaches-Assoc. w/High Blood Pressure	Sinusitis (Smokes 2 Pk. a Day for 30 Yrs.)	1970-Appendectomy 1971-Started Treatment for Hypertension
1177	49	None	None	None	None	None
1178	34	None	None	None	None	None
1179		None	Indigestion - Ulcer 2 Yrs. Ago	None	None	None
1180	33	Has Dry Skin	None	Occ. Insomnia	None	Hypertension 1957-Hemorrhoidectomy
1181	48	None	None	None	Occ. S.O.B.	None
1182	52	None	None	None	None	1976-Cataract-Right Eye 1929-Scarlet Fever 1968-Reconstruction of Knee Joint - Tendon Transplant
1183	47	None	None	None	Occ. Sinusitis (Smoked Pipe for 20 Years)	1964-Boil-I & D
1184	54	Has Had Rash Off & On - Hands - 35 Yrs. (Hyperhidrosis)	None	None	None	Hepatitis-12 Yrs. Ago.
1186	49	None	Occ. Indigestion	Headaches-Assoc. w/Sinus	Sinus- ? Deviated Septum	1966-Benign Cyst Rem. from Rgt. Bronchial Tube (Smoked 20 Yrs.-Quit 1975)

COMPLAINTS

		SKIN RASHES	GI SYMPTOMS	NEUROLOGIC	RESPIRATORY	OTHER
1187	45	None	Occ. Diarrhea	None	Slight Hay Fe[illegible] Has Sinusit[illegible]	1972-Kidney Stone [illegible]
1188	50	None	None	None	Chronic Cough Cigarettes - for 23 Yrs. S.O.B. After Exertion	[illegible]
1189	59	None	None	None	Chronic Cough Smokes 1 Pk. Day	[illegible] Yrs. Ago [illegible] gnant) (Probable Skin [illegible])
1190	33	(Some Skin Dis- coloration-Chest) Seborrheic Derma- titis	Occ. Indigestion	None	None	Prostatitis - 2 Yrs. Ago
1154	61	Skin Itching - Allergic to Soap (Detergent)	None	None	None	195[illegible]-Hernia Repair
1191	41	None	None	None	None	195[illegible]-Rgt. Shoulder Recon- struction [illegible] Excision Mole - Left Chest Area
1192	49	None	None	None	None	1946-Hepatitis
1193	45	None	None	None	None	Hypertension-Since Age 24 Bilateral Inguinal Hernia - 1966-Left 1973-Right 1962-Duodenal Ulcer 1966-Exc. Sebaceous Cyst
1194	19	Mild Acne of Back	None	None	None	1963-Hepatitis 1974-Small Cyst Removed

13. Biochemical Findings

Elevations in the serum lipids - either triglycerides, cholesterol, or both - and/or positive correlations between the levels of such serum lipids and those of PCBS, represent the most widely reported biochemical finding in populations exposed to PCBS. Such reports raise two questions: First, are the reported lipid elevations best correlated with the PCBS themselves, or with chloracnegenic impurities in the PCBS (such as PCDFS), or with compounding factors such as alcohol, drug use, or obesity? Second, are the observed correlations between lipid and PCB levels caused by the action of PCBS on the liver (e.g., leading to increases in lipoprotein synthesis and enzyme activation) or are they caused by the action of the serum lipids on the PCBS (leading to shifts in distribution from adipose tissue reservoirs into the serum)?

In this section, we present the biochemical findings in detail, with emphasis on blood lipids, fasting blood glucose and body weight; the statistical methods used in their analysis; and the results of such statistical analyses.

A. Methods

The clinical chemistries of this [illegible] were performed on serum shipped to Metpath, Inc., Teterboro, N.J. Although individual erroneous values have occasionally occurred as the result of improper sample preparation, inadequate volume requiring dilution, or laboratory error, in general, such errors have been readily detected and, in a statistical sense, the results appear reliable. Metpath provides a computerized summary on a monthly basis which compares the values obtained over a given period of time with their normal ranges adjusted for age and sex. This analysis, however, treats all the variables as normally distributed.

The present analysis focuses primarily on the 1979 data, where reasonably reliable data for serum PCBs are available. Analysis of the 1976 data is at present limited to selected variables. As the result of study dropouts, incomplete data (primarily serum Aveclor 1260 values) and the occurrence of intercurrent disease, comparable data was available in both 1976 and 1979 on 126 males and 33 females. Twelve individuals were omitted because of diabetes (5), alcohol problems (2), nonfasting samples (3) and serious medical problems (post-op pi itary tumor, epileptic under intensive medication) at the time of the study. One subject has a familial form of hypertriglyceridemia and was also omitted.

Serum lipids, including total lipid, triglycerides and cholesterol, were determined in 1976. Because of analytical difficulties the measurement of total lipids was omitted by the vendor in 1979. An analysis of the data for total lipids in 1976 shows some subjects where the sum of the triglycerides and cholesterol values exceeded the total lipid value. Because of such errors and the lack of replication in 1979 the total lipid measurements have been discarded except for Figure 9.3.

Serum triglyceride values in 1979 were reported up to 400 mgms/100 ml, the balance being reported as >400 mgms/100 ml. Numerical values for levels greater than 400 were reported in 1976, although their accuracy is probably questionable. In manipulating the triglyceride values we have used the maximum likelihood method of evaluating such data (see below) or have omitted them from the analysis.

B. Results

Variable Distributions and Means

The principal biochemical variables measured in 1979 are listed in Table 13.1. Distributions were determined in each case and logarithmic transformation carried out as indicated. We differed from Smith et al. with respect to the distribution of direct bilirubin and creatinine which appeared normal in our population, rather than lognormal as described by them. The lognormally distributed variables are given as geometric means. The range of the data is given by ± twice the standard deviations and compared with the Metpath standard ranges unadjusted for sex and age. The elevations in serum triglycerides and cholesterol are apparent. In addition, the data described below indicate elevations in fasting blood sugar in a significant segment of the population. The standard ranges for SGOT, SGPT and SGGTP given by Metpath are somewhat higher than those given by others, e.g., the Merck Manual. Using the Metpath standard there appears to be an elevation in the serum SGPT, but not GGTP. However, many of the liver enzyme levels are a function of age and sex.

Serum Triglycerides

In Figure 13.1 histograms are used to compare male and female values for 1976 and 1979. In both sexes the values have increased in the three year period as measured by a paired t-test. For the males the

Table 13-1

BIOCHEMICAL VARIABLES 1979 (N = 172)

Table 13.1. Measured biochemical variables for Study Group I in 1979. N = 172. Means ±SD given as logarithms for lognormal distributions and converted to arithmetic values ($\overline{X}$). Range is given as ±2 SD. Standard values from the analytical laboratory (Met-path, Inc.). Starred values exceed the laboratory range. Distributions at variance with Smith et al. are also starred. Normal ranges for SGOT, SGPT and GGTP at variance with other values in the literature.

	Mean	± SD	Distribution	$\overline{X}$	Range (± 2 SD)		Standard
Triglycerides	2.16	0.226	Lognormal	144.5	51	409*	50–200 mg/DL
Cholesterol	238.2	50.2	Normal	238.2	138	339*	125–300 mg/DL
Blood Sugar	1.995	0.058	Lognormal	98.9	75.7	129.1*	65–130 mg/DL
Uric Acid	6.03	1.29	Normal	6.03	3.5	8.6	3.3–8.9 mg/DL
Total Bilirubin	−0.214	0.165	Lognormal	0.61	0.29	1.31	0.1–1.4 mg/DL
Direct Bilirubin	0.141	0.075	Normal*	0.141	0	0.29	0–0.4 mg/DL
SGOT	1.449	0.143	Lognormal	28.1	14.6	54.3	1–50 IU/L
SGPT	1.538	0.163	Lognormal	34.5	16.3	73.1*	1–55 IU/L
GGTP	1.200	0.266	Lognormal	15.9	4.7	54.0	1–70 U/L
Alk. Phosp.	1.466	0.123	Lognormal	29.2	16.6	51.5	15–55 IU/L
LDH	173.3	31.4	Normal	173.3	111	236	97–250 IU/L
Total Prot.	7.32	0.47	Normal	7.32	6.4	8.3	6.2–8.3 gm/DL
Albumin	4.42	0.38	Normal	4.42	3.7	5.2	3.8–5.1 gm/DL
Globulin	2.93	0.43	Normal	2.93	2.1	3.8	2.1–4.0 gm/DL
A/G Ratio	1.54	0.29	Normal	1.54	1.0	2.1	1–2.2
BUN	1.23	0.11	Lognormal	16.9	10.2	28.2	7–28 mg/DL
Creatinine	1.33	0.20	Normal*	1.33	0.9	1.7	0.8–1.8 mg/DL
BUN/Creat. Ratio	1.11	0.12	Lognormal	12.9	7.4	22.4	–
Na	139.4	2.33	Normal	139.4	135	144	134–146 mMol/L
K	4.42	0.45	Normal	4.42	3.5	5.3	3.4–5.4 mMol/L
Chloride	103.8	3.3	Normal	103.8	97	110	96–109 mMol/L
Calcium	9.67	0.42	Normal	9.67	8.8	10.5	8.7–10.5 mg/DL
Phorphorous	2.85	[illegible]	Normal	2.85	2.0	3.7	1.9–4.3 mg/DL
Magnesium	1.91	0.15	Normal	1.91	1.6	2.2	1.6–2.3 mEq/L

*Distributions differ from Smith et al.

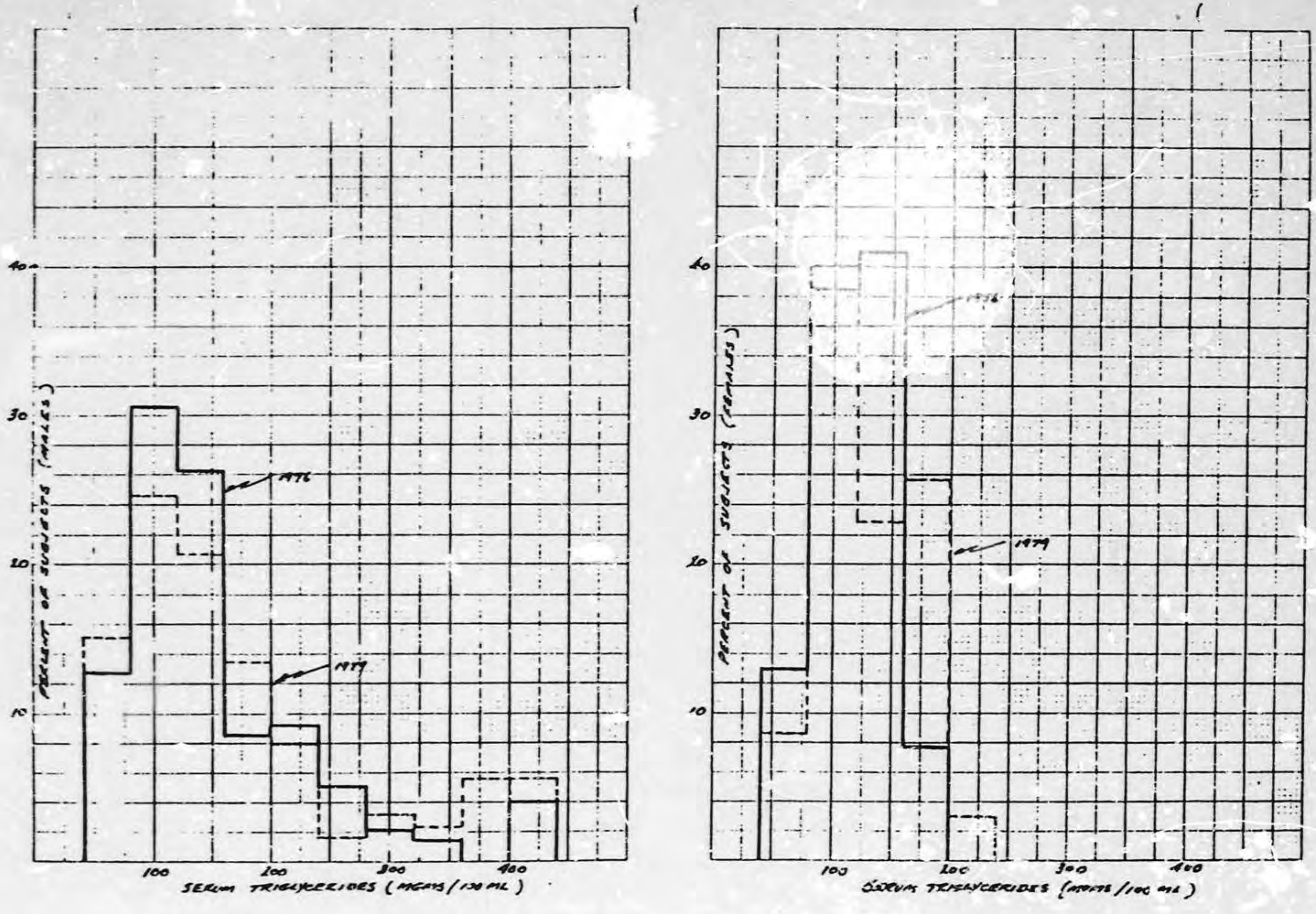

Figure 13.1. Histograms of serum triglyceride values in 1976 and 1979 in Study Group 1. Males and females given separately. Levels increased significantly between 1976 and 1979 by paired t-test.

increase is significant at nearly the one percent level (t = 2.53, d.f. = 126); for the females the increase is significant at nearly the five percent level (t = 1.92, d.f. = 34). These increases occurred primarily following the PCB ban in mid-1977.

Serum triglyceride values (± the standard error) for males are shown in Figure 13.2 arranged in 5-year age groups. They are compared to the means (solid line), medians (dotted line) and the 5th and 95th percentile found in the Lipid Research Clinics prevalence study.[1] The averages for the age groups are well within the 95th percentile and appear to conform to the general curvature of this standard. Although the analytical methodology in our study (enzymatic method using a discrete analyzer) was different than that used in the Lipid Research Clinics Program (Technicon Autoanalyzer; fluorimetric method), it is unlikely that methodology could account for the elevations observed.

The data for the male subjects are presented also using logarithmic transformation because of the highly skewed distribution which normally occurs with triglyceride values and which is apparent in the LRCP data. The data points are somewhat erratic which is probably a function of the extremely high values found in some age groups and would be further elevated if accurate numerical values above 400 mgms/100 ml were available. In the statistical analysis logarithmic transformation will be used for the triglyceride values. Hulley et al.[2] have recently used a

1 Plasma Lipid Distributions in Selected North American Populations: The Lipid Research Clinics Program Prevalence Study. Circulation 60. 427-439, 1979.

2 Hulley, S.F., Rosenman, R.H., Bawal, R.D., and R.J. Brand. The association between triglycerides and coronary heart disease. N.E.J. Med. 302: 1383-9, 1980.

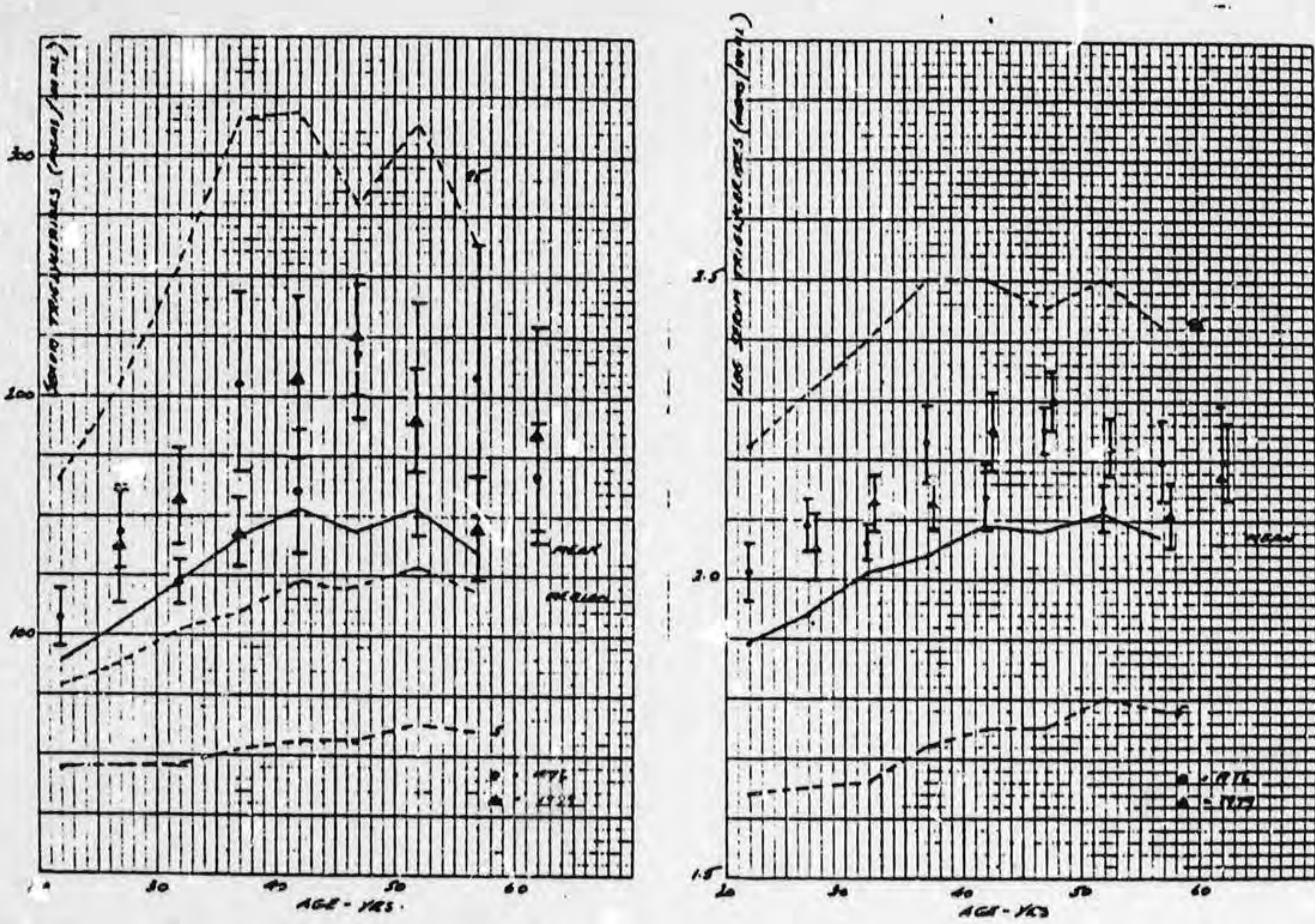

Figure 13.2. Comparison of serum triglycerides levels in Study Group 1 with the Lipid Research Clinics Program standards as a function of age for males. Solid circles = 1976: solid triangles = 1979; vertical bars = ± S.E. for 5-year age groups. Left panel: solid bar = arithmetic mean; dotted lines = median and 5th-95th percentiles. Right panel shows logarithmic transformation. Solid line = geometric mean; dotted lines = 5th and 95th percentiles. The serum triglycerides for all ages in both 1976 and 1979 are elevated compared to the standard population means.

similar procedure in a study of the association of triglycerides and coronary heart disease. Persuasive evidence was not found.

The Lipid Research Clinics study indicated a significant elevation of serum triglyceride levels for females taking estrogens. In Figure 13.3 the solid lines (marked E) are the curves associated with estrogen use and the dotted lines the nonusers. The eight subjects composing the data points at 33 and 37 years have complicated gynecological histories. All are married but in the interim between 1976 and 1979 there have been two hysterectomies and three tubal ligations. Prior to 1976 all but five apparently took estrogens for birth control and since then 2 have continued on estrogens. In addition, six of the eight subjects are judged obese.

The elevated triglyceride values found in these young women are therefore interpreted as reflecting estrogen medication and/or obesity and are seen to fall closer to the estrogen standard curve for females.

The elevations in serum triglyceride levels in our population, therefore, appear to be primarily confined to the males.

In Figure 13.4 is shown a scatter plot of the individual male serum triglyceride values in 1976 and 1979. Using the LPCP standards two populations can be defined; those within the 5th and 95th percentile (normal range) and those elevated above the 95th percentile. Histograms of these normal and abnormal populations are shown in Figure 13.5. In both cases the crossover point has been in the region of 200 mgms/100 ml. There are 6-10 percent false negative values, primarily among the younger employees, and 4-6 percent false positives,

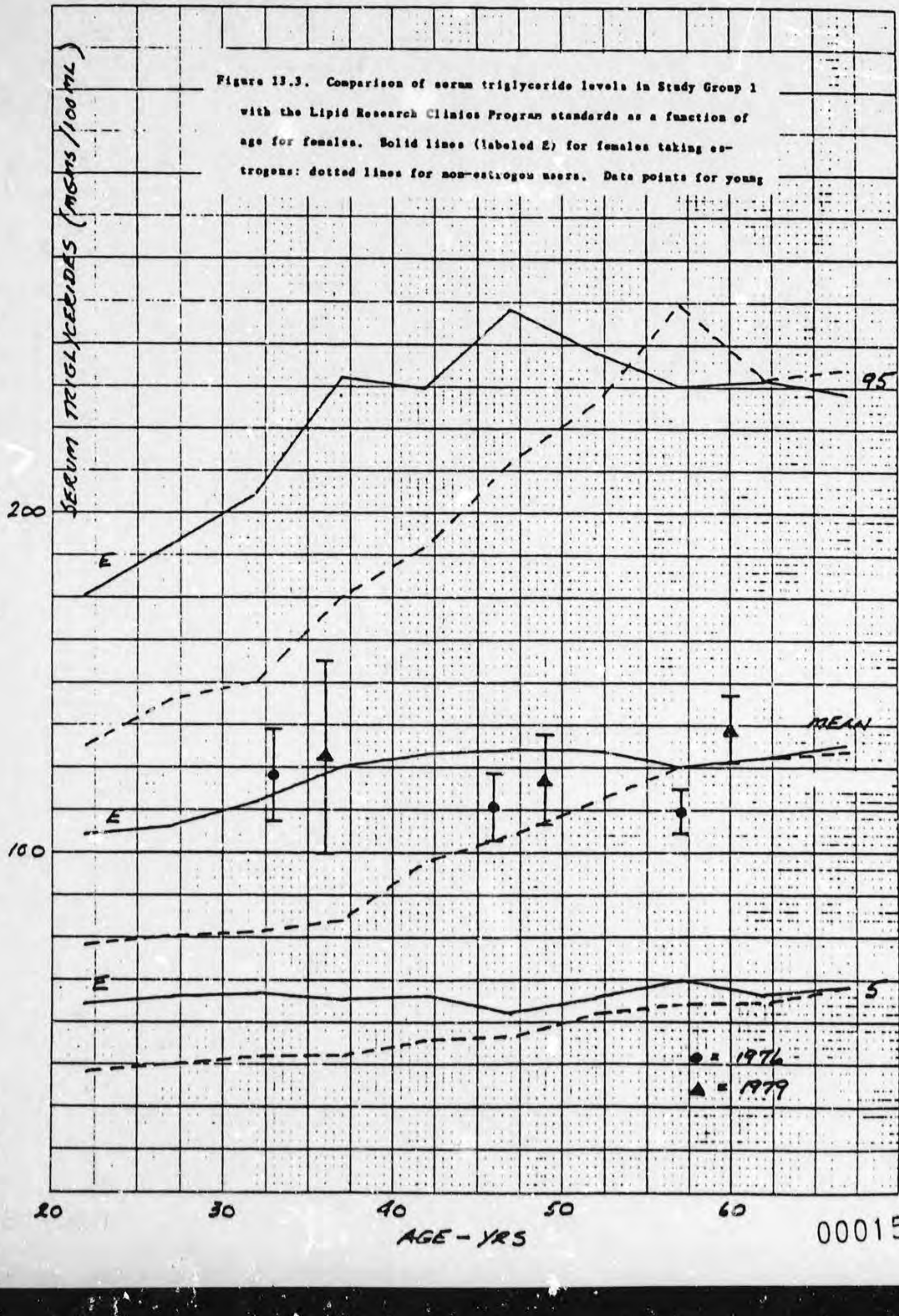

Figure 13.3. Comparison of serum triglyceride levels in Study Group 1 with the Lipid Research Clinics Program standards as a function of age for females. Solid lines (labeled E) for females taking estrogens: dotted lines for non-estrogen users. Data points for young

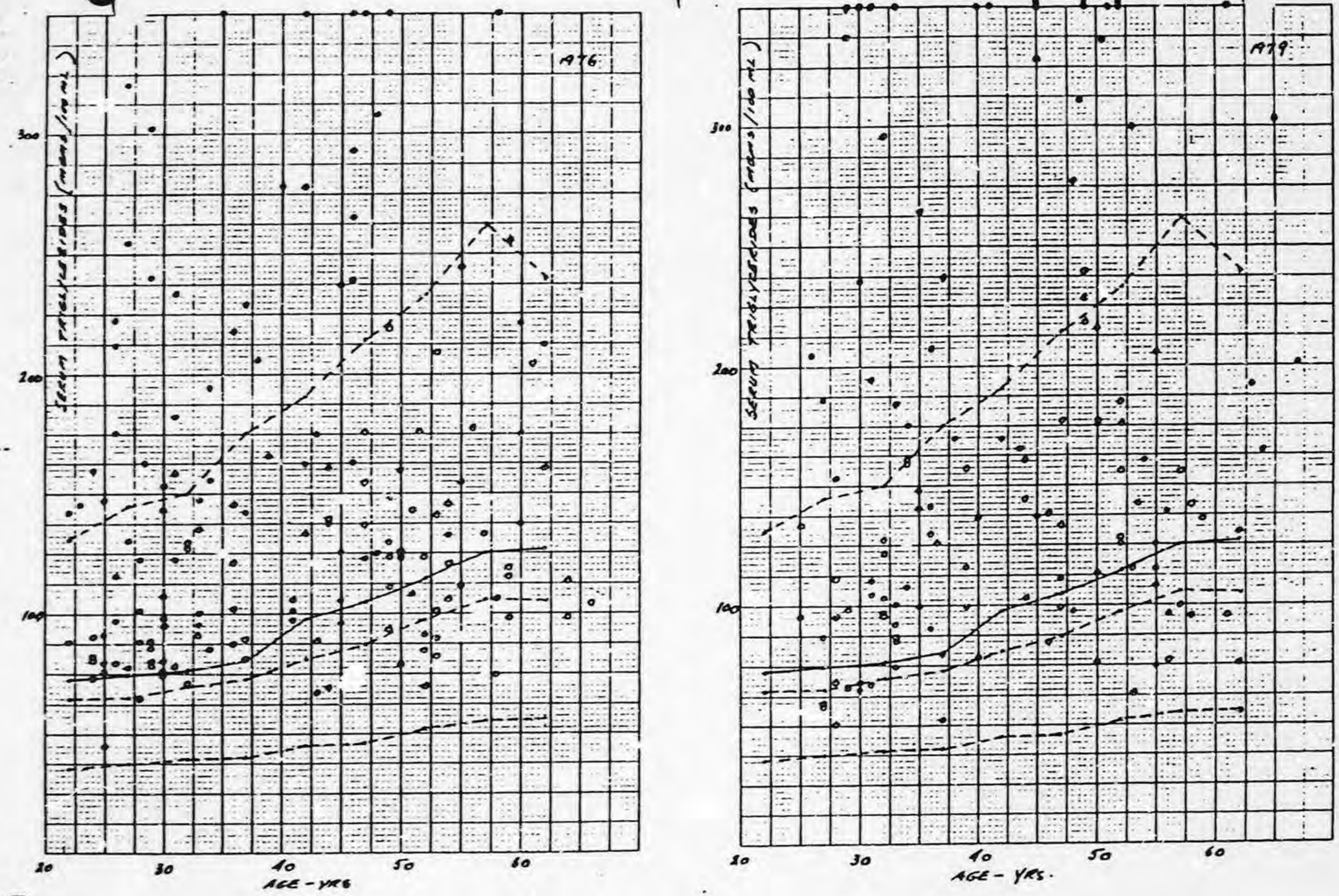

Figure 13.4. Individual serum triglyceride values for Study Group 1 males as described in Figure 13.2. Values for 1976 and 1979 shown in separate panels. Values above the 95th percentile = solid circles.

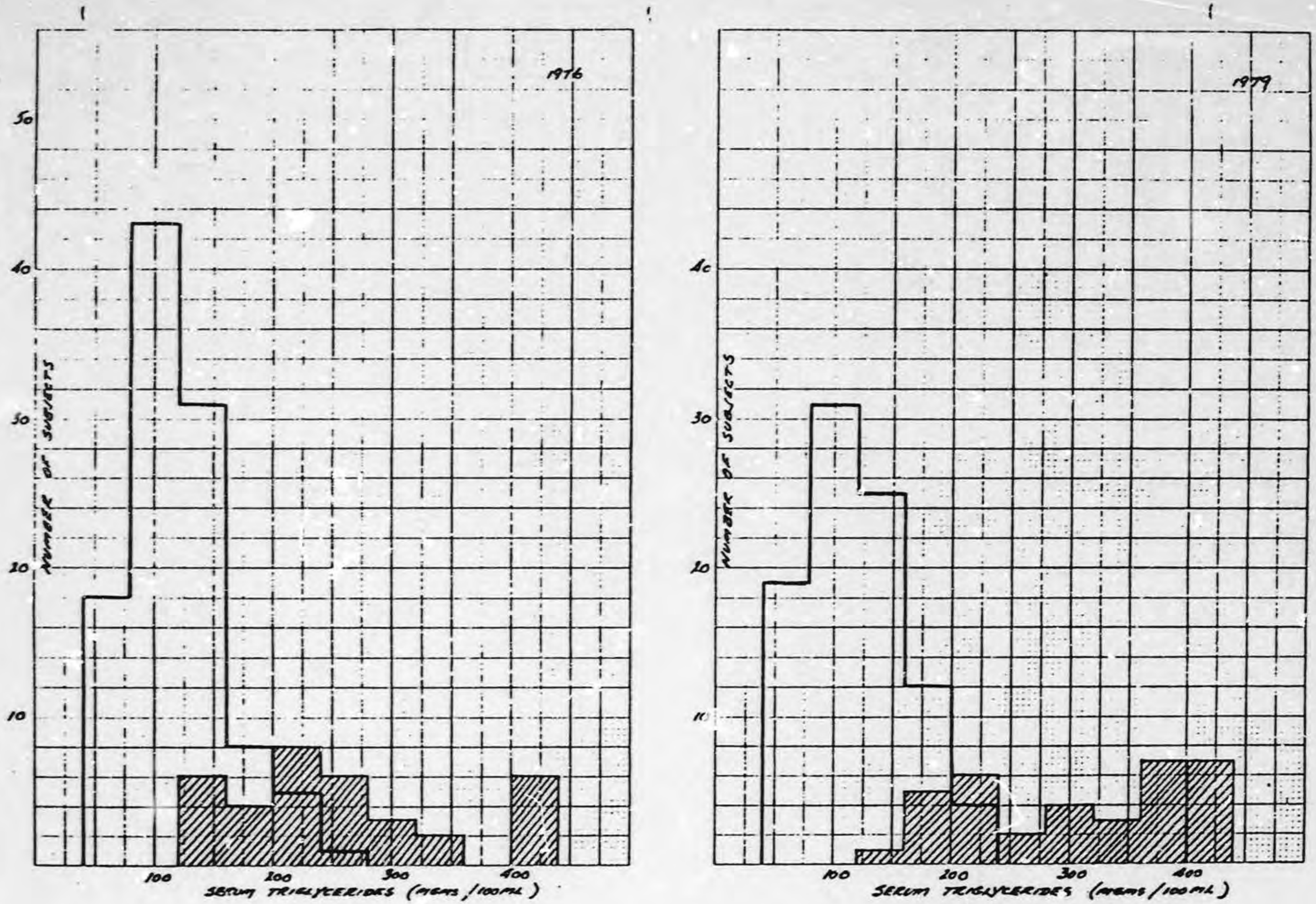

Figure 13.5. Histograms for data in Figure 13.4. Cross-hatched histogram is for values above the 95th percentile. Normal/abnormal cutoff value = approximately 200 [illegible]s/100 ml.

primarily among the older employees.

Twenty-five percent of a total of 141 male employees (35 subjects) were judged abnormal by the LPC criteria in 1976. Of these one subject was not repeated, 24 subjects remained elevated and 10 declined to the normal range in 1979. Eleven subjects showed elevations outside the normal range in 1979. The total study population declined to 126 (10.6%) in 1979 so that the percent of abnormals rose to 28 percent.

Serum Cholesterol

Histograms for the serum cholesterol values for males and females in 1976 and 1979 are shown in Figure 13.6. The mean value for each sex declined between 1976 and 1979, a decline which was statistically significant at the 1 percent level. Notice that the arithmetic means and the medians are nearly identical indicating a predominantly normal distribution.

The values are plotted as a function of 5-year age increments in Figure 13.7. Except for a few points involving individuals with very high or low values, the data fall within the 50th and 95th percentile of the Lipid Research Clinics standard. For the females the values are elevated beyond what might be expected from estrogen use. In contrast to the triglycerides, the LRC standards show the mean equidistant from the 5th and 95th percentile attesting to the normal distribution of this data.

In assembling the data for the males in Figure 13.7 the procedure consisted of averaging the data by age cells in 1976 and then averaging

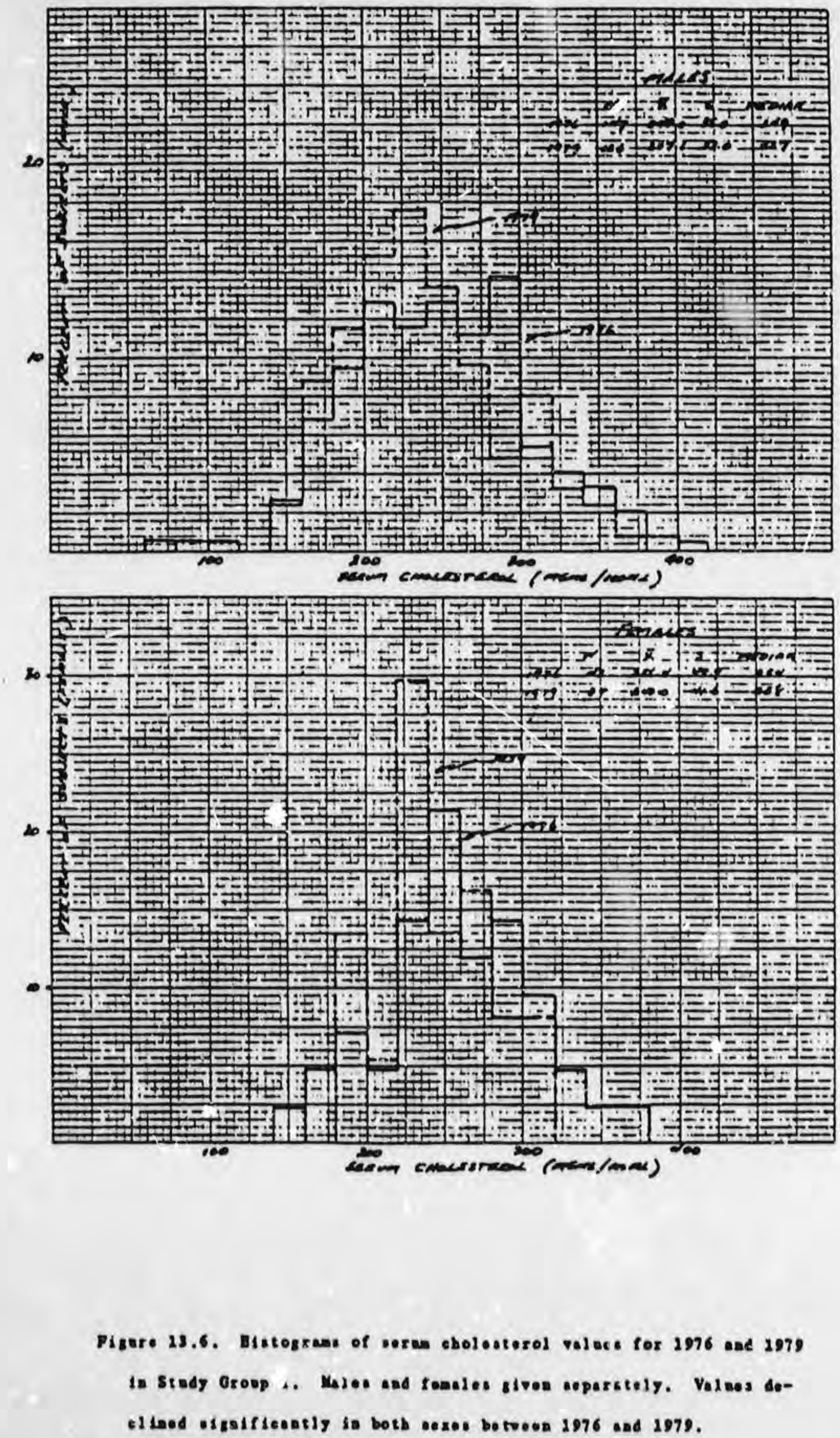

Figure 13.6. Histograms of serum cholesterol values for 1976 and 1979 in Study Group [illegible]. Males and females given separately. Values declined significantly in both sexes between 1976 and 1979.

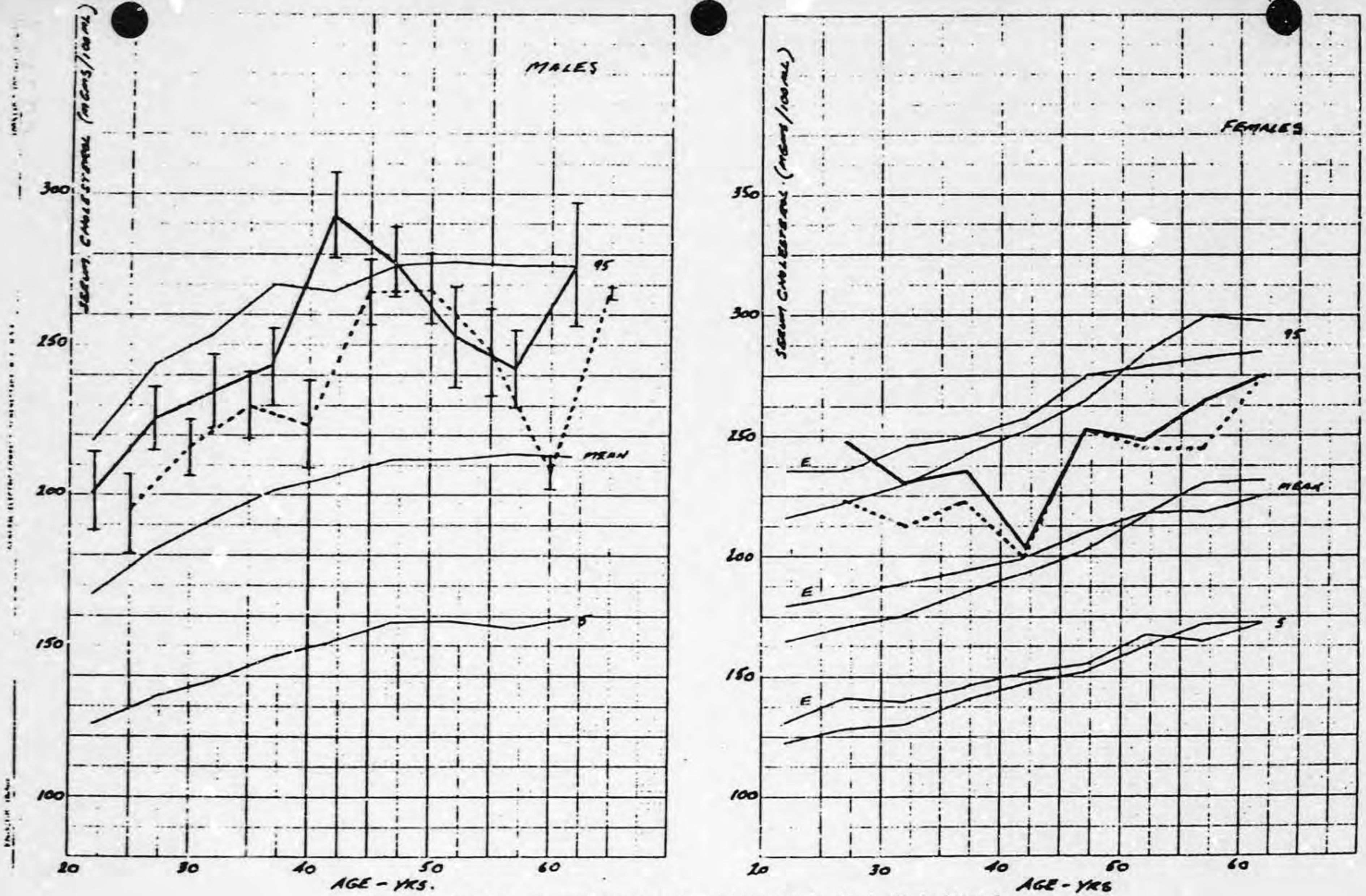

Figure 13.7. Comparison of serum cholesterol levels in Study Group 1 with the Lipid Research Clinics Program standards as a function of age and sex. Data the same as Figure 13.2 except serum cholesterol values are normally distributed. Values are elevated for both sexes at all ages over the standard population means. The effect of estrogens on the female standard (curve E) is small.

the same group in 1979, moving the point 3 years on the age axis. Thus, there appears to have been a systematic decline in average cholesterol in all age groups among males. The number of individuals with values greater than 300 mgms/100 ml, however, remained relatively constant at about 14 percent of the total population.

Fasting Blood Glucose

Histograms of the fasting blood glucose values in 1976 and 1979 are compared in Figure 13.8. A paired t-test of 162 values showed that the apparent decline in 1979 was statistically significant ($t = 3.162$, $p < 0.001$).

Although the distribution is apparently lognormal (Figure 13.9), careful examination reveals an inflection point at around 70 percent of the population. The 1976 distribution has been analyzed graphically by the method of Harding[3] as modified by Cassie[4] using the cumulative percentage plot (Figure 13.10) and can be construed as bimodal with one population mean at 103 mgms/DL and another at 122 mgms/DL. The data suggest a cut-off at 115 mgms/DL (83 percent).

The Metpath standard indicates 130 mgms/DL as an upper limit of normal. However, using the 115 mgms/DL cut-off, 42 individuals at one time or another over the 3-year period (1976-1979) showed an elevation in fasting blood sugar. Five individuals had been or were diagnosed as

3 Harding, J.P. The use of probability paper for the graphic analysis of polymodal frequency distributions. J. Marine Biol. Assoc. (U.K.) **28**: 141-153, 1949.

4 Cassie, R.M. Some uses of probability paper in the analysis of size frequency distributions. Australian J. Marine and Freshwater Res. **5**: 514-522, 1954.

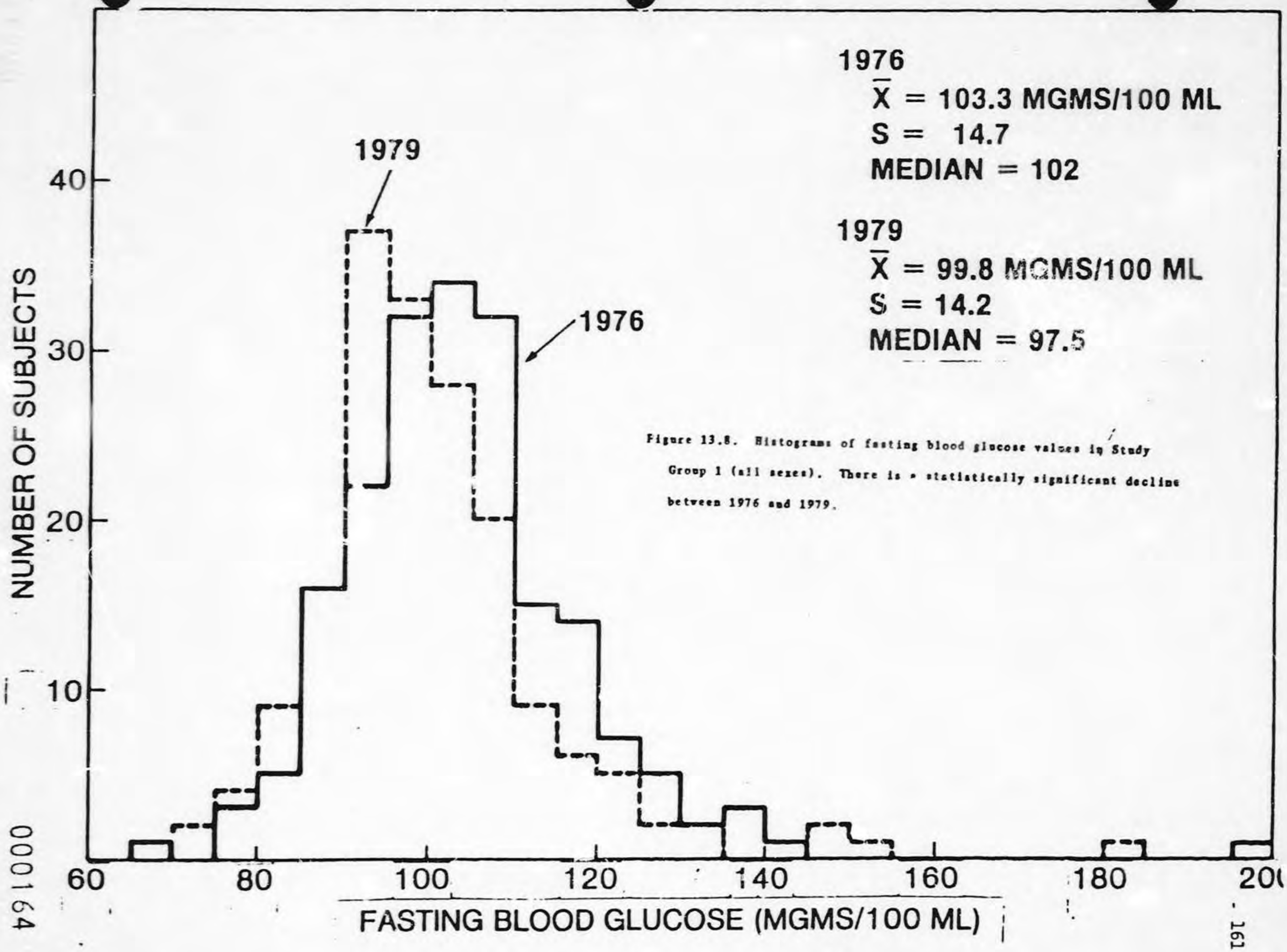

Figure 13.8. Histograms of fasting blood glucose values in Study Group 1 (all sexes). There is a statistically significant decline between 1976 and 1979.

Figure 13.9. Cumulative percentage plot of log fasting blood glucose (1976). The data are lognormally distributed. Two outliers are identified by circles which have been omitted in the analysis. Inspection shows an inflection at 80 percent.

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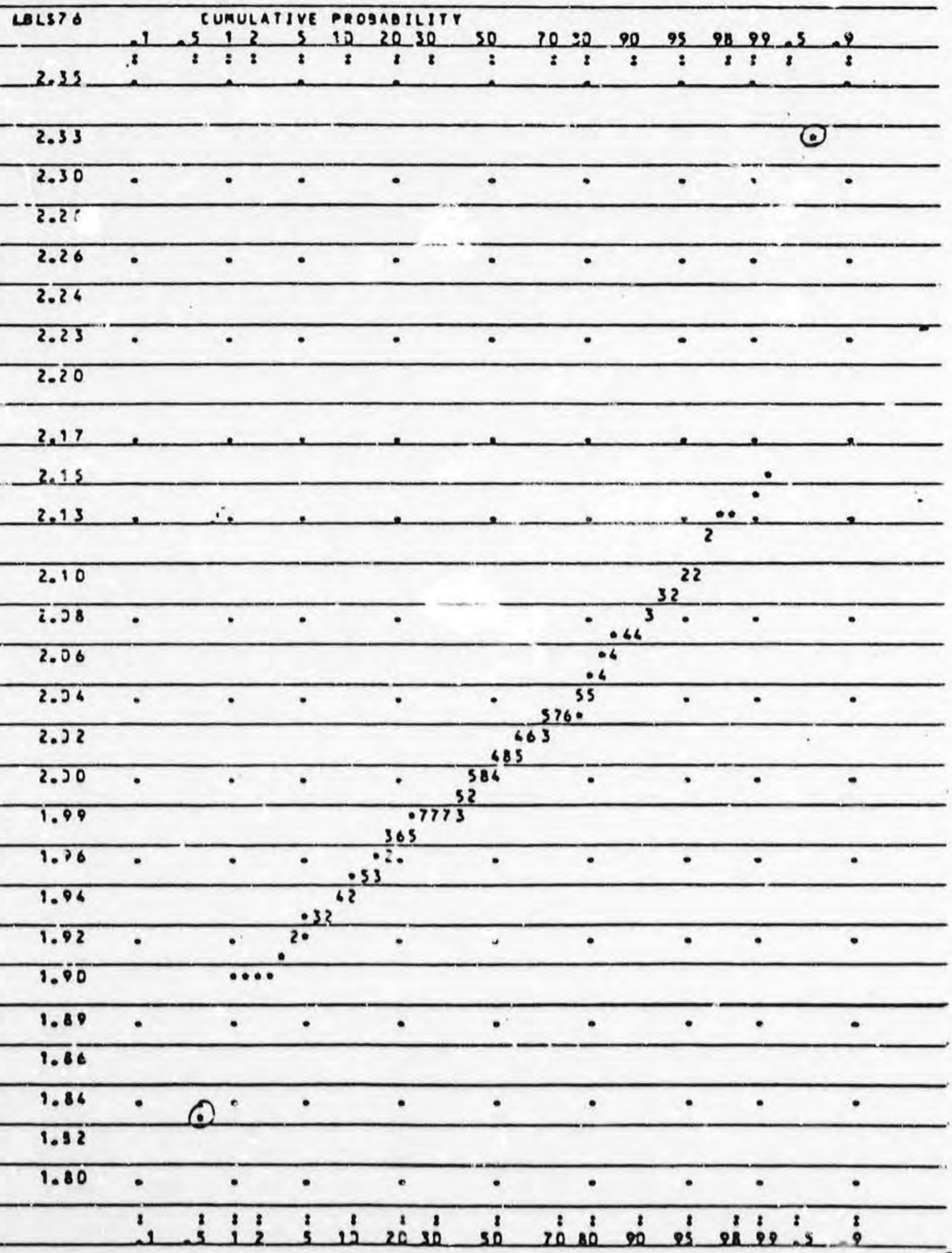

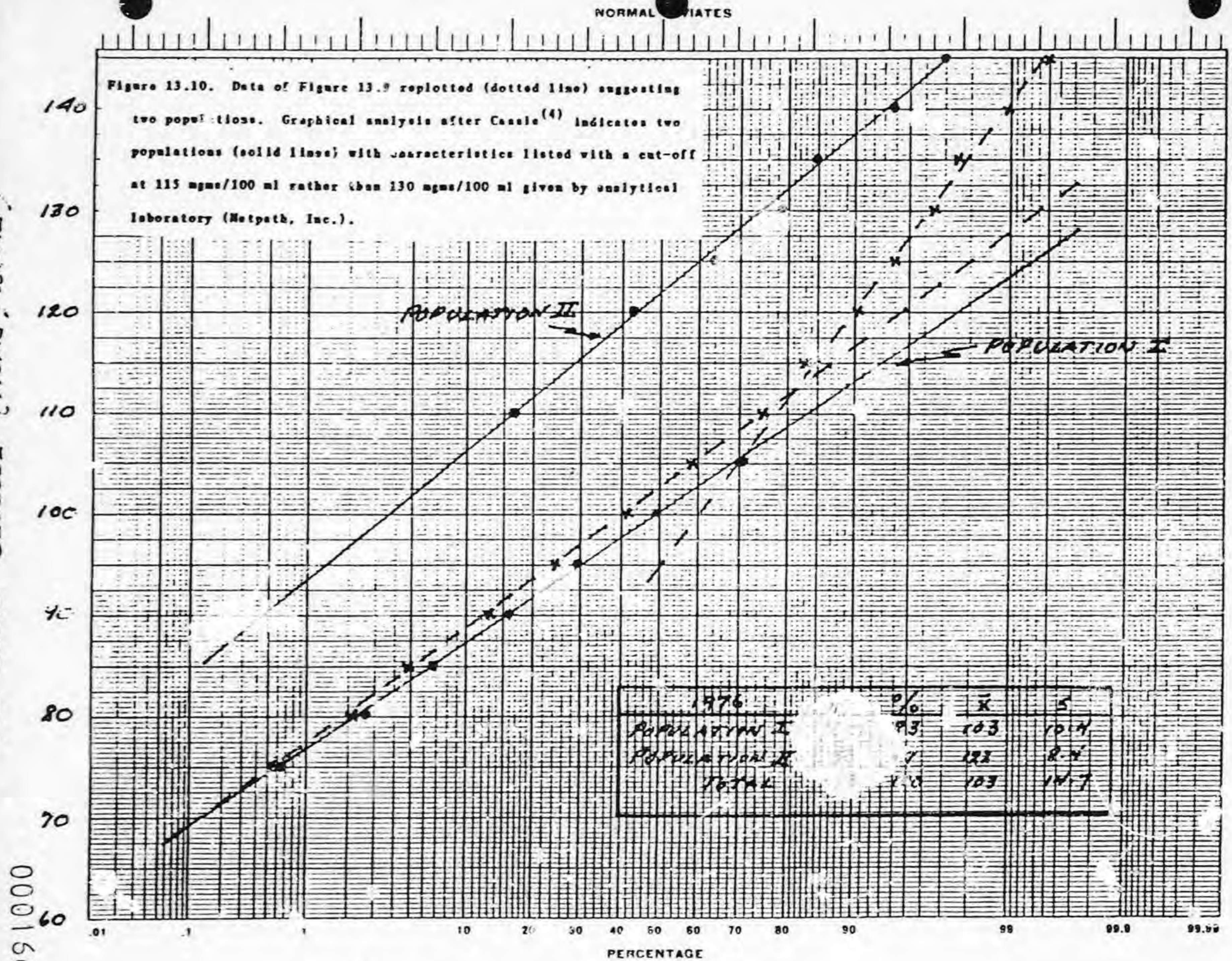

Figure 13.10. Data of Figure 13.9 replotted (dotted line) suggesting two populations. Graphical analysis after Cassie[4] indicates two populations (solid lines) with characteristics listed with a cut-off at 115 mgms/100 ml rather than 130 mgms/100 ml given by analytical laboratory (Metpath, Inc.).

diabetics. Two individuals had alcohol problems. One individual had had a pituitary tumor treated surgically but remained obese. Three subjects were thought to be non-fasting. One individual was an epileptic under intensive medication.

C[illegible]ng these subjects yields a group size approximately as calculated (30 vs 33). Post-prandial glucose levels were determined at two hours following a high fat, high carbohydrate meal in 19 remaining subjects and these values were within normal limits. In general, subjects showing one fasting sample which was elevated had prior or subsequent samples within criteria. Only two subjects had repeated fasting elevations but normal post-prandial values.

Fasting blood glucose levels increased with age at the rate of 1.87 mgms/DL per decade (Figure 13.11) which is in accord with the literature.(5) Glucosuria was not observed.

Uric Acid

Serum uric acid levels in this population were normally distributed with a mean of about 6 mgms/100 ml, and showed essentially no change between 1976 and 1979. Although the normal textbook range is 3-7 mgms/100 ml, the Metpath range extends from 3-9 mgms/100 ml rising with age. Our values, therefore, lie within the normal range for their procedure.

5 Merck Manual 13th Ed. 1977, pg. 1291.

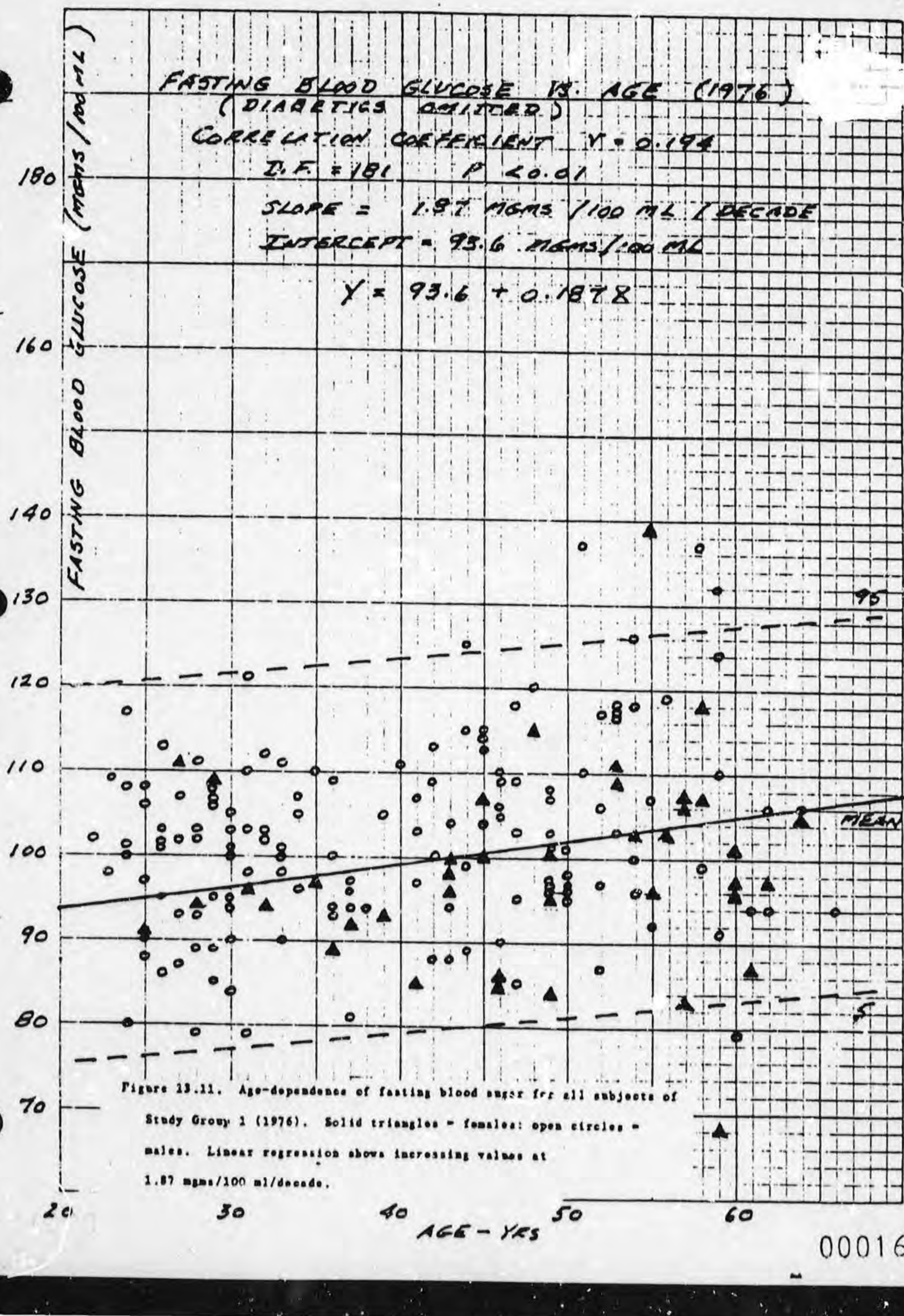

Figure 13.11. Age-dependence of fasting blood sugar for all subjects of Study Group 1 (1976). Solid triangles = females: open circles = males. Linear regression shows increasing values at 1.87 mgms/100 ml/decade.

Measures of Body Weight

Body weight and height were measured without shoes in indoor clothing as a part of the medical examination in 1976 and 1979. One of us (M.R.) evaluated each individual with respect to body frame (small, medium, and large). Preemployment weight and height was also available on 91 subjects, primarily employees hired within the last ten years, although the nature of the dress on these occasions is not known.

We have evaluated body weight in terms of relative weight, as the body mass index and as total body fat.

Relative Body Weight

Body weight at constant body height (determined in 1979) and frame were compared to the maximum ''desirable'' body weight and the average body weight as a function of age using the Metropolitan Life Insurance data.(6) While such differences provide a measure of under- and overweight, they are not a good guide to obesity.(7,8) However, when the same standard is used throughout, changes in body weight and population weight distribution can be assessed.

The results of a new study (Build and Blood Pressure Study, Association of Life Insurance Medical Directors, Society of Actuaries, 1979)

6 New Weight Standards for Men and Women. Statistical Bulletin, Metropolitan Life Insurance Co. 40: 1-4, Nov.-Dec. 1959.

7 Grande, F. Assessment of body fat in man. In Obesity in Perspective. Proceedings of the Conference. Ed. G.A. Bray et al. U.S. Printing Office, Stock No. 017-053-00046-9. pp. 189-203.

8 Seltzer, C.C., Stoudt, H.W., Bell, B., and J. Mayer. Reliability of relative body weight as a criterion for obesity. Am. J. Epidem. 92: 339-350, 1970.

will probably result in an upward revision of these 1959 standards of from 10 to 12 lbs.

Histograms for the male and female populations in 1976 for body weight and height are shown in Figure 13.12. The data are normally distributed. The population weight mean for males was elevated with respect to mean height and age (+8 lbs) but that of the female population was not. Figure 13.13 shows the individual subjects' weight as compared to the ''desirable'' weight for their height and frame. Fifty percent of the total population were above the range for large framed individuals.

Preemployment weight was obtained on 91 individuals. In Figure 13.14 histograms are used to compare these preemployment weights (heavy line) with those found in 1976 (light lines) in terms of the standard ranges of desirable weights. At employment 51 percent of the males and 62 percent of the females had body weights within or greater than the desirable range. In 1976, 80 percent of males and 85 percent of females were at or above the standard. A paired t-test showed this weight gain to be significant at the 0.005 level. The weight gain continued between 1976 and 1979 for males ($t = 2.83$, d.f. = 128; $p < 0.005$) but not for females ($t = 0.82$; d.f. = 35, $p > 0.20$). Linear regression (Figures 13.15 and 13.16) showed that the weight gain in males was correlated with service time ($r = 0.37$, d.f. = 90, $p < 0.01$) rather than age ($r = 0.07$, $p > 0.2$). In those gaining weight the increase appeared in the first 5 years of employment. While male body weight remained elevated in all groups, body weight in females fell to a minimum between age 40 and 50, perhaps as the result of conscious dieting (Figures 13.17

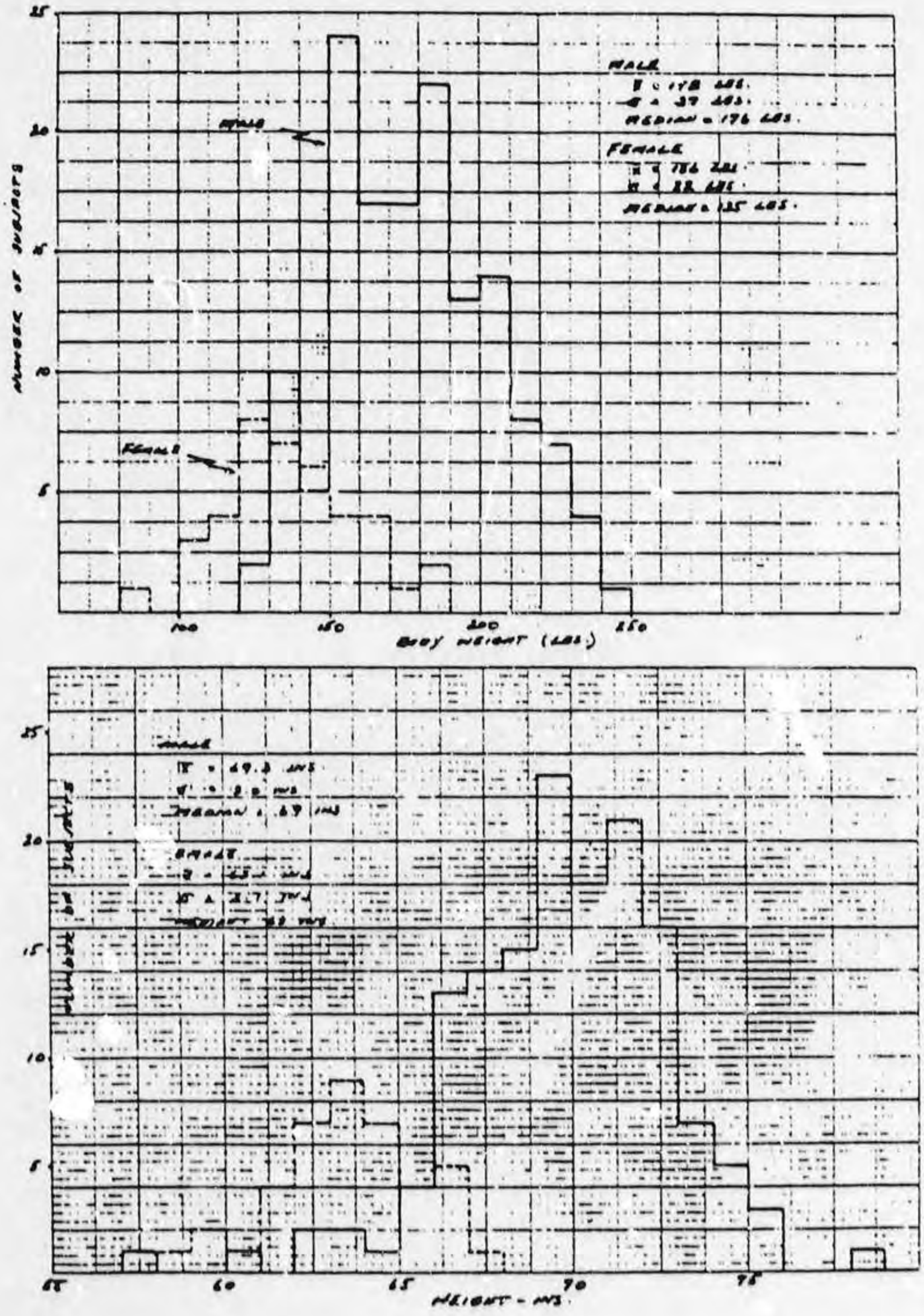

Figure 13.12. Histograms of body weight and height for males (solid line) and females (dotted line) of Study Group 1 in 1976. Male and female means and standard deviations given in the insets. Means and medians are equivalent indicating normal distributions.

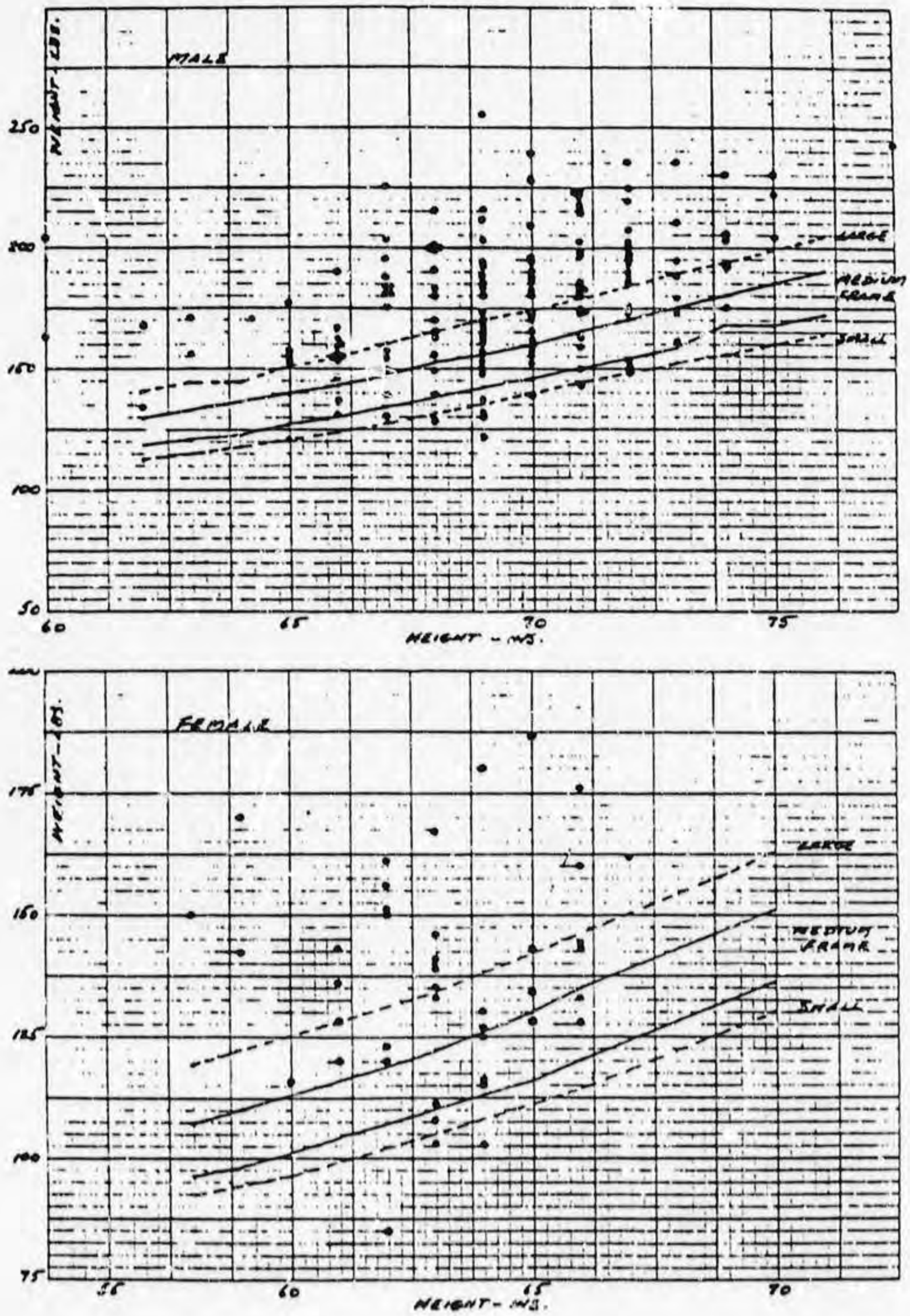

Figure 13.13. Comparison of individual body weights with ''desirable'' body weights for individual height and frame. Ranges for medium frame (solid lines): upper limit for large frame and lower limit for small frame (dotted line). Fifty percent of workers were above the range for large framed individuals.

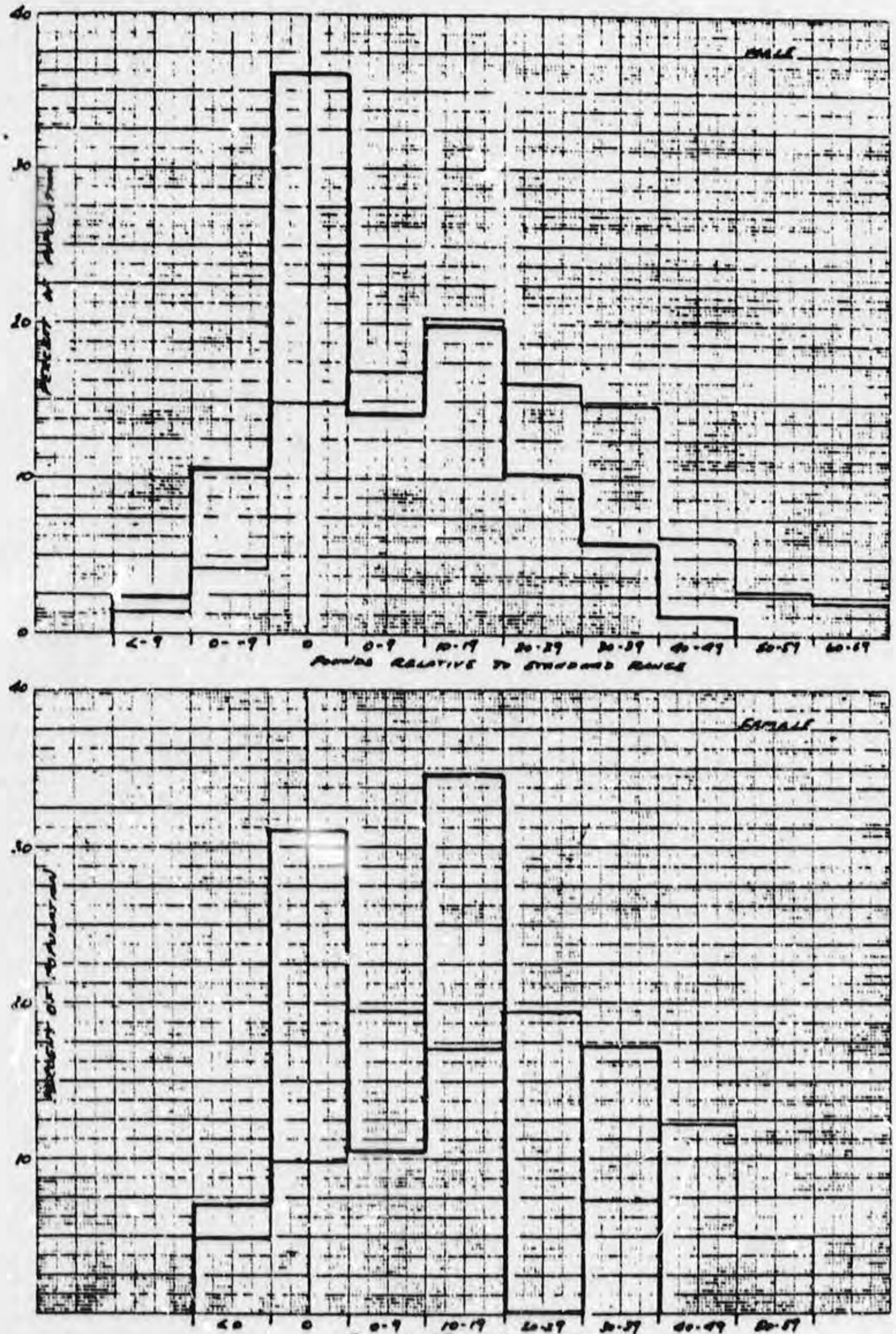

Figure 13.14. Comparison of preemployment body weight (heavy line) with body weight in 1976 (light line) in terms of standard ranges of ''desirable'' weight. The study population shows a significant weight gain for both males and females.

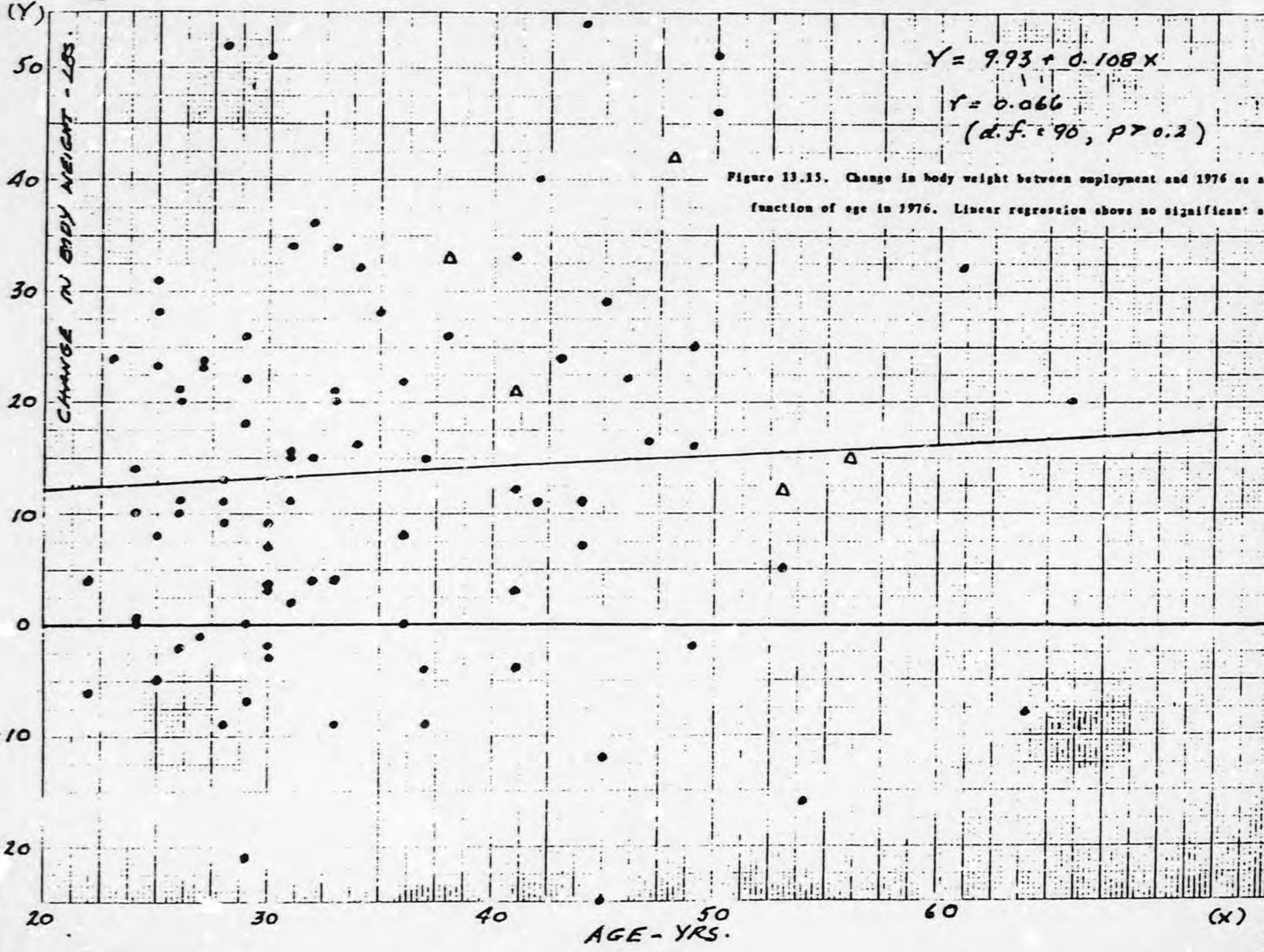

Figure 13.15. Change in body weight between employment and 1976 as a function of age in 1976. Linear regression shows no significant age

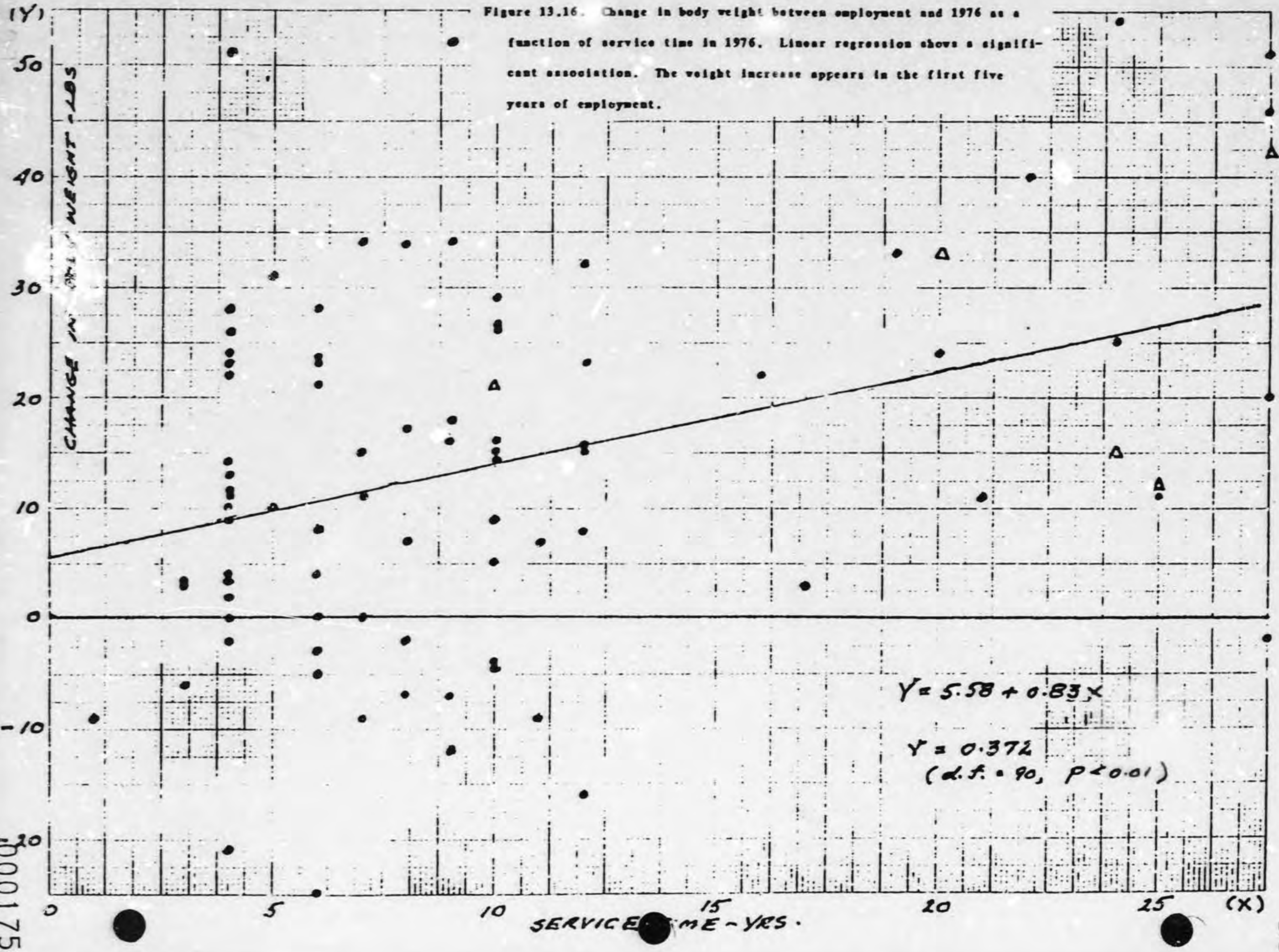

Figure 13.16. Change in body weight between employment and 1976 as a function of service time in 1976. Linear regression shows a significant association. The weight increase appears in the first five years of employment.

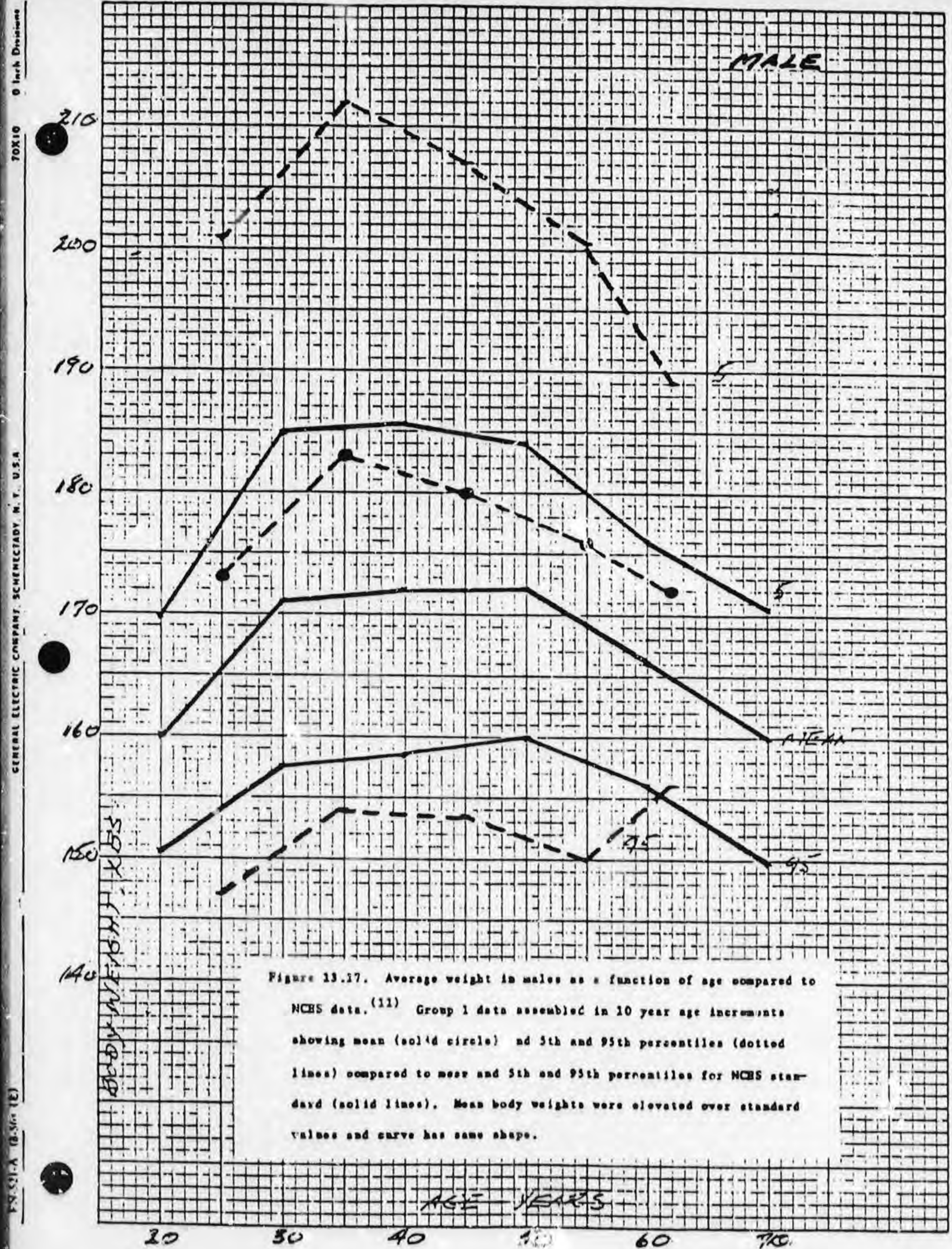

Figure 13.17. Average weight in males as a function of age compared to NCHS data.[11] Group 1 data assembled in 10 year age increments showing mean (solid circle) and 5th and 95th percentiles (dotted lines) compared to mean and 5th and 95th percentiles for NCHS standard (solid lines). Mean body weights were elevated over standard values and curve has same shape.

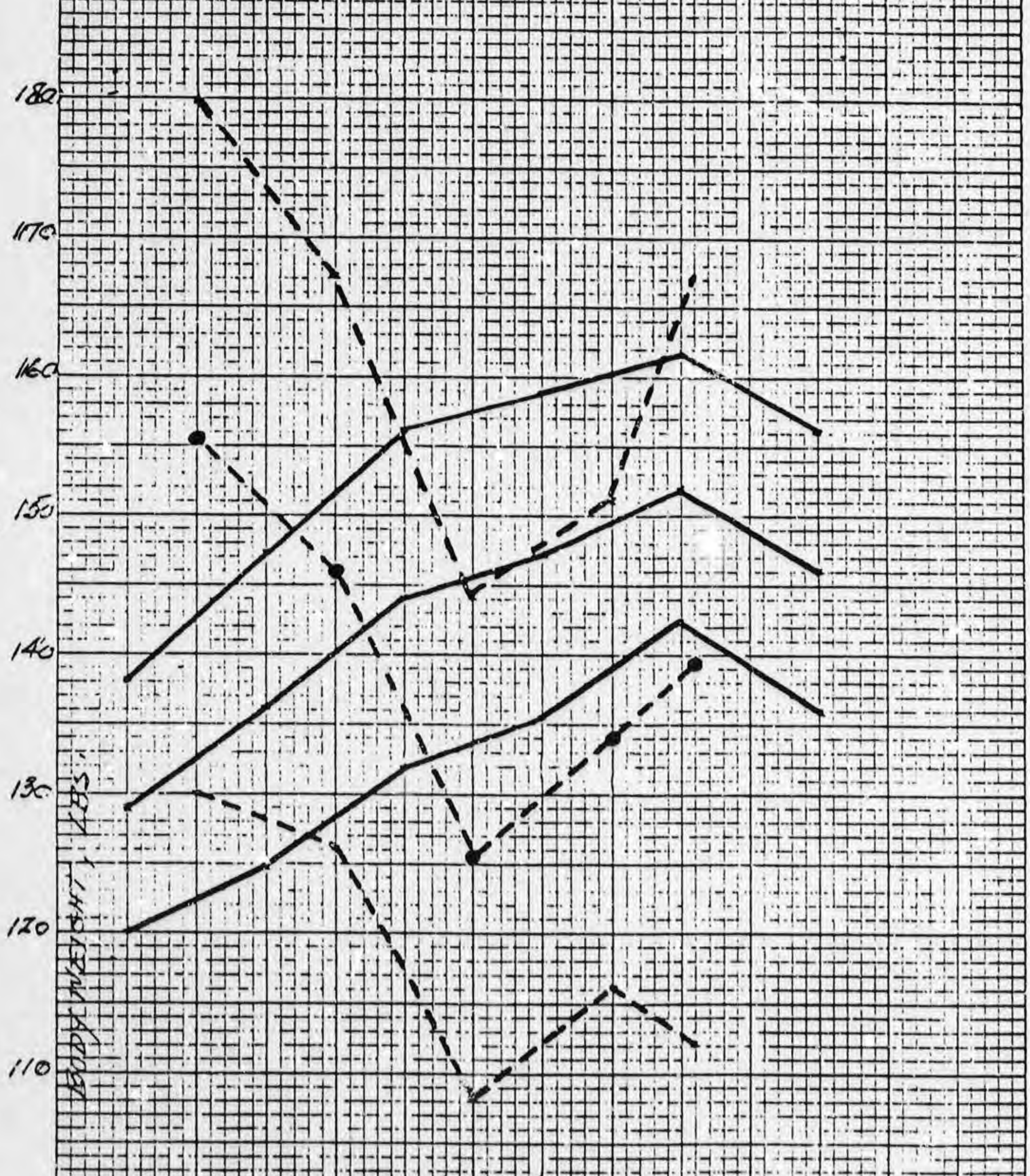

Figure 13.18. Average body weight in females as a function of age compared to NCHS data.[11] Legends the same as Figure 13.17 but showing reduction in average body weight with age in the study group.

and 13.18), when compared to U.S. vital statistics in 1966.[9]

The relative body weight data is summarized in Table 13.2 in terms of percent of both the 1959 national averages and desirable weight.[6]

Body Mass Index

We have calculated the body mass index (Quetelet index) for our subjects using W/H^2 for males[9] and $W/H^{1.5}$ for females[9,10] This index is highly correlated with weight and generally independent of height. Although good correlations have been obtained between this index and skinfold thickness ($r = 0.8$) and body density, it probably is not superior to relative body weight as a predictor of fatness.[7]

The body mass index calculations for both males and females and the population are shown in Table 13.3. There was a statistically significant increase in this index in males between employment and the 1976 study and the means were significantly higher than those calculated from the insurance averages (MLI Std (6)). The increase for females was significant at the 3 percent level. In 1976 and in 1979 the increases were not significantly different, however, from the insurance averages. Figure 13-19 shows the relation between the preemployment and 1976 values as compared to the insurance averages calculated for each individual.

9 National Center for Health Statistics 1966. U.S. HEW Vital Health Stat. Ser. 11 (4).

10 Keys, A., Fidanza, F., Karvonen, M.J., et al. Indices of relative weight and obesity. J. Chronic Dis. 25: 329-343, 1972.

11 Kreiss, K., Zack, M.W., Kimbrough, R.D., et al. Association of blood pressure and polychlorinated biphenyl levels. J.A.M.A. 245: 2505-2509, 1981.

Table 13.2

RELATIVE BODY WEIGHT

Table 13.2. Relative body weight in males and females of Study Group 1 as a percent of both national averages and desirable weight.[6] Details of calculation in Table. The percent expected is calculated from Tables I and II of Ref. 6 indicating that the males are slightly over and the females slightly under these standards. Preemployment calculations are incomplete.

	N	Over/Underweight* (% of Nat. Averages)	Over/Underweight** (% of Desirable Wt.)	% Expected*** Over/Underweight
Males				
Preempl.	91		2.12 ± 10.9	
1976	152	5.00 ± 13.9	11.1 ± 12.6	6.16 ± 6.9
1979	136	2.76 ± 14.2	9.57 ± 12.9	6.93 ± 6.5
Females				
Preempl.	29		5.82 ± 12.6	
1976	42	−1.49 ± 18.4	14.9 ± 17.9	17.2 ± 8.7
1979	38	−3.24 ± 20.1	14.1 ± 20.2	18.6 ± 7.9

* $\frac{\text{Observed body weight} - \text{Metrop. Life average body weight}}{\text{Metrop. Life average body weight}} \times 100$ from Table I of Ref. 6.

** $\frac{\text{Observed body weight} - \text{Metrop. Life max. desirable weight}}{\text{Metrop. Life max. desirable weight}} \times 100$ from Table II of Ref. 6.

*** $\frac{\text{Metrop. Life average body weight} - \text{Metrop. Life max. desirable body weight}}{\text{Metrop. Life max. desirable body weight}} \times 100$

Table 13.3

BODY MASS INDEX

Table 13.3. Mean body mass index (±S.D.) for Study Group 1. Males = W/H^2; females = $W/H^{1.5}$. The index has been calculated from Ref. 6 (MLI STD). A t-test of the means shows both males and females to be significantly elevated between employment and 1976 and that the males are significantly elevated over the MLI standard.

	Male ($W/H^2 \times 100$)			Female ($W/H^{1.5} \times 100$)		
Preemployment	3.43 ± 0.38	$n = 91$		25.48 ± 3.29	$n = 29$	
			$t = 5.25$			$t = 1.91$
1976	3.75 ± 0.50	$n = 152$		27.43 ± 4.68	$n = 42$	$p < 0.03$
			$t = 4.32$			$= 0.62$
MLI STD	3.57 ± 0.11	$n = 152$		27.90 ± 1.21	$n = 42$	
1979	3.70 ± 0.52	$n = 136$		27.29 ± 5.17	$n = 38$	
			$t = 7.36$			$t = 1.16$
MLI STD	3.60 ± 0.086	$n = 152$		28.24 ± 0.97	$n = 42$	

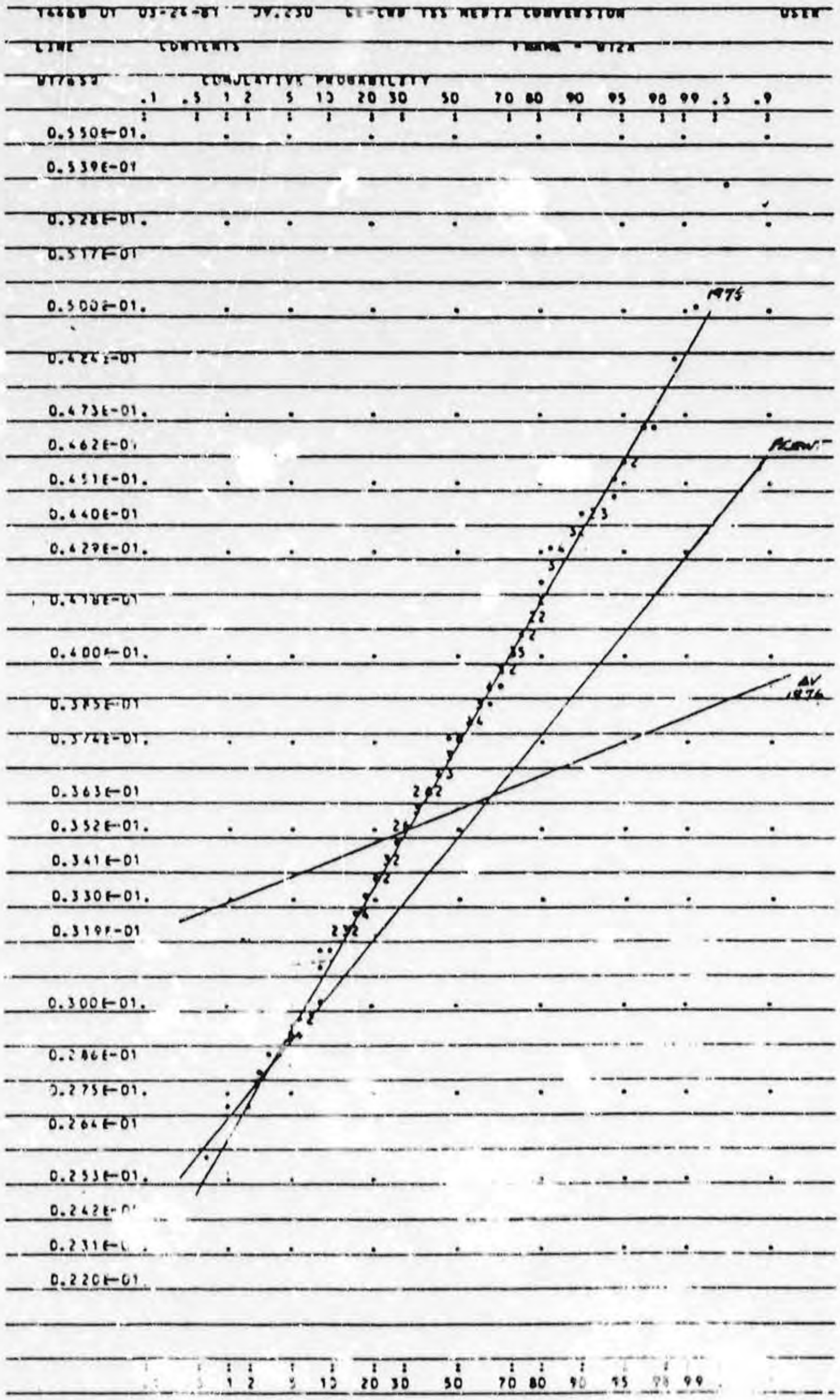

Figure 13.29. Cumulative percentage plot of body mass index for males in 1976. Data for preemployment (PREWT) and calculated from Ref. 6 (AV 1976) overlaid for comparison. Ordinate should be multiplied by 100.

Figure 13.20 shows the individual values for the body mass index for males as a function of age. They are compared to a study by Khosla and Lowe[12] of 5000 workers in an electrical industry in England in 1967. The insurance averages[6] are shown as a dotted line. Our data appear to be encompassed by ± 2 SD. The elevation of the body mass index (3.75) over the insurance averages (3.57) and that of Khosla and Lowe (population mean = 3.50) suggests that any overweight in our population cannot be due to a greater height.

Body Fat

Table 13.4 shows the results of the body fat calculation as the percent of body weight at employment and in 1976 and 1979. Body fat calculated from insurance average weights for height and age are comparable. These data (and the preceding discussion) indicate that our population conformed in most respects with insurance population averages particularly in view of the impending revisions. While our population exceeded desirable weight levels, the average weight gains represented only 65 percent chemical fat[13] and were modest. A portion of the population, however, was obese by all standards.

We have used body fat as a percent of body weight as an independent variable in the statistical analysis of our PCB data which we now consider.

12 Khosla, T. and C.R. Lowe. Indices of obesity derived from body weight and height. Brit. J. Prev. Soc. Med. 21: 122-128, 1967.

13 Siri, W.E. The gross composition of the body. Advan. Biol. and Med. Physics 4: 229-280, 1956.

Figure 13.20. Body mass index for males as a function of age for Study Group 1 compared to data of Ref. 12 (means ± SD). Dotted line is calculated from MLI standards (Ref. 6). The study group data is encompassed by ±2 SD of Ref. 12.

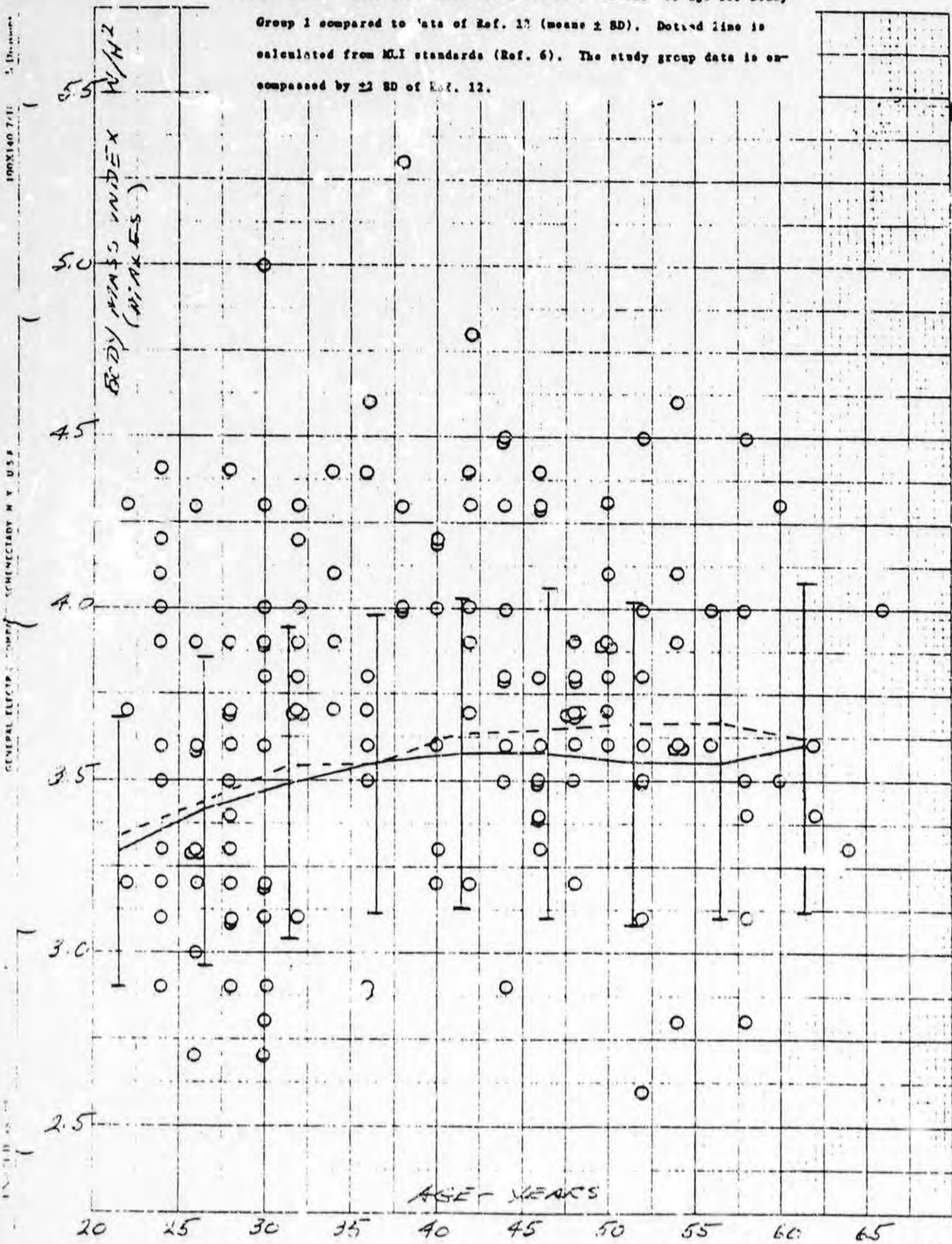

Table 13.4

BODY FAT AS A PERCENT OF BODY WEIGHT FOR STUDY POPULATION 1

Table 13.4. Body fat as a percent of body weight for Study Group 1 for males and females. Also shown are the changes in percent body fat between preemployment and the study periods (1976 and 1979) and between the study periods. The greatest change occurred between employment and 1976.

	Males		Females		Total	
	N	$\bar{X} \pm SD$	N	$\bar{X} \pm SD$	N	$\bar{X} \pm SD$
Preemployment	91	16.0 ± 4.8	29	18.1 ± 4.4	120	16.5 ± 4.8
1976	152	21.9 ± 7.0	42	21.6 ± 5.7	174	21.9 ± 6.7
1979	136	21.7 ± 6.9	38	21.8 ± 6.2	174	21.7 ± 6.7
PreE−1976	91	+4.8 ± 4.6	29	+3.4 ± 3.9		
PreE−1979	83	+4.9 ± 4.3	27	+3.2 ± 5.8		
1976−1979	136	−1.4 ± 2.6	38	−1.5 ± 3.2		

C. Statistical Analysis

Statistical analyses were performed on a Honeywell 600/6000 computer using available time-sharing applications programs provided by the manufacturer. The programs were periodically checked using library guide examples[14] or problems in textbooks. Many of the variables are lognormally distributed, and this assumption was validated usng the W-test[15] incorporated in these programs.

Major use was made of a versatile general statistical package STATPAC[16] which has some of the capabilities of the more widely used BMDP series. This package has been used for distribution plotting, cross-plots, and multiple linear regression, including both forward and backward step-wise regression. The capability is available to handle censored data by maximum likelihood analysis[17] which we have used in the analysis of the p, p - DDE values of 1976 and the 1979 serum triglyceride data.

A principal problem in statistical analysis in much medical and epidemiological research is the occurrence of multicollinearity, or linear dependence among the regressor variables. The listing of the

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14 Honeywell Series 600/6000 Time Sharing Applications Library Guide Vol. II. Statistics. Honeywell Information Systems, Inc. 1973 (DA 44).

15 Hahn, G.J. and S.S. Shapiro, Statistical Models in Engineering. John Wiley, New York, 1967.

16 Nelson, W.B., Morgan, C.B., and P. Caporal, 1979 STATPAC Simplified-A Short Introduction to How to Run STATPAC, a general statistical package for data analysis. GE Corporate R and D Report No. 78CRD276, December 1978.

17 Nelson, W.B., Estimation of Product Life Distributions by Maximum Likelihood Analysis of Censored Data. GE Corporate R and D Report No. 77CRD119, May 1977.

major variables of this study (Table 6.1) indicated that there are almost as many variables as individuals, particularly when subsets of the population are considered. When the technique of multiple linear regression is applied, it is often found that parameter estimates and generality of the estimated model may be affected more by the multicollinearity existing among the variables than by the relationship existing between the response variable and the regressor variables.

A model of this type is described by Mason, et al.[18] as ''overdefined.'' The analytical approach requires either (a) model redefinition with some of the variables debted, (b) preliminary investigation using only subsets of the variables, or (c) a principal components analysis in an attempt to choose the variables to remove from the model. In Table 6.1 variables of this study are presented in physiological groups. We propose here to examine the relationships between the population variables and metabolic parameters with a view to the revision of the results by subsequent studies of the other variable groups in accordance with (b) above.

Even within variable subsets multicollinearity persists, so we have investigated principal components (factor) analysis to help choose subset variables for deletion from the model.

There are other sources of multicollinearity. The sampling process may introduce collinearity, for instance. Our study population, however, is not unique and others studying the relations of PCBs to regressor variables have also encountered similar problems. In addition,

18 Mason, R.L., Gunst, R.F. and J.T. Webster, Regression Analysis and Problems of Multicollinearity, Commun. in Statistics 4(3):277-292, 1975.

there may be physical constraints on the model irregardless of the sampling technique employed, particularly with respect to the many biochemical measurements. Mason[18] cites examples in chemical analysis where the sum of certain constituents in a solution must always be constant, although the value of the individual constituents may vary. In our case this question arises with respect to individual serum lipids (triglycerides + cholesterol) versus the sum of the lipids, the Aroclor 1242 and 1260 values vs. their sum (total PCBs), and the individual crystalloids versus osmolarity.

Another approach to the problem of multicollinearity is an augmentation of the data base, particularly when collinearity is related to sampling. In epidemiology this approach may not be feasible either because exposure conditions have changed, or the population cannot be recovered. Our two sequential examinations may permit some estimate of the stability of the collinearities over time in the same population. For the present, analysis has only been extended to the 1979 data.

Factor Analysis

The correlation coefficient matrix for 27 variables is shown in Table 13.5. Coefficients ≤ 0.3 are circled for convenience. In the column for sex (and elsewhere in this analysis) the data coding resulted in negative values associated with females in this population. High correlations were evident between certain pairs of variables: total bilirubin/direct bilirubin (0.75), SGOT/SGPT (0.76), globulin/A/G ratio (-0.88), and BUN/BUN/creatinine ratio (0.83).

TABLE 13.5. CORRELATION COEFFICIENT MATRIX

Table 13.5. Correlation coefficient matrix of biochemical parameters of Study Group 1 in 1979. Major possible associations (R ⩾ 0.30) are encircled for easier identification. Suspected collinearitis have very high values of R (0.7-0.9).

	SEX	SER	PFAT	TRI	CHOL	BLS	URIC	TBIL	DBIL	SGOT	SGPT	GGTP	ALK
SEX	1.00												
SER	0.03	1.00											
PFAT	0.63	0.24	1.00										
TRI	0.10	0.13	0.20	1.00									
CHOL	0.04	0.30	0.20	0.54	1.00								
BLS	0.02	0.27	0̄.18	0.26	0.13	1.00							
URIC	−0.47	−0.10	−0.10	0.32	0.09	0.01	1.00						
TBIL	−0.26	−0.25	−0.20	0.10	0.03	0̄.13	0.26	1.00					
DBIL	−0.12	−0.16	−0.13	−0.09	0.01	0̄.01	0.13	0.75	[illegible]				
SGOT	−0.12	0.04	0.05	0.16	0.09	0.07	0.27	0.18	0.09	1.00			
SGPT	−0.19	0.01	0.09	0.27	0.15	0.12	0.39	0.18	0.05	0.76	1.00		
GGTP	−0.32	0.12	−0.09	0.36	0.30	0.16	0.42	0.21	0.11	0.44	0.47	1.00	
ALK	0.01	0.11	0.09	0.30	0.18	0.02	0.04	0.04	0̄.03	0.17	0.17	0.29	1.00
LDH	0.09	0.03	0.18	0.20	0.12	0̄.13	0.16	0.10	0̄.05	0.20	0.20	0.15	0.20
TPRO	−0.05	0̄.02	0.05	0.37	0.26	0.03	0.31	0.22	0.14	0.36	0.38	0.36	0.25
ALB	−0.17	0̄.15	0̄.26	0.05	0̄.04	0̄.02	0.23	0.22	0.25	0.15	0.13	0.09	0.03
GLOB	0.07	0.16	0.21	0.33	0.28	0.14	0.16	0̄.05	0̄.12	0.28	0.27	0.34	0.26
A/GRAT	0̄.10	0̄.19	0̄.25	0̄.22	0̄.22	0̄.16	−0.04	0.18	0.22	0̄.14	0̄.12	0̄.24	0̄.18
BUN	0̄.13	0.21	0.17	0.21	0.23	0.22	0.23	0̄.01	0.02	0.07	0.17	0.09	0.02
CRE	0.32	0.29	0̄.06	0.01	0.01	0̄.10	0.34	0.19	0.09	0.34	[illegible]	0.28	0.02
B/CRAT	0.06	0.15	0.19	0.21	0.23	0.28	0.02	0̄.51	0̄.05	0̄.12	0.0[illegible]	0̄.06	0.02
NA	0.14	0.10	0.15	0̄.02	0̄.01	0.02	0̄.12	0̄.10	0.04	0.03	0̄.03	0.04	0.10
K	0̄.13	0.12	0̄.08	0.02	0.02	0.08	0̄.02	0̄.09	0̄.09	0̄.13	0̄.02	0.05	0.02
CHL	0.17	0̄.06	0.11	0̄.02	0̄.06	0.07	0̄.16	0̄.25	0̄.20	0̄.18	0̄.01	0̄.18	0.18
CAL	0̄.05	0.09	0̄.03	0.21	0.19	0.14	0.30	0.09	0̄.05	0.22	0.25	0.20	0̄.05
PHOS	0.15	0̄.04	0.03	0̄.08	0̄.06	0̄.10	0̄.12	0̄.11	0̄.19	0.04	0.02	0̄.06	0.02
MAE	0̄.01	0.13	0.06	0.18	0.15	0.04	0.05	0.05	0̄.07	0.13	0.07	014	0.27

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LDH	TPRO	ALB	GLOB	A/GRAT	BUN	CRE	B/CRAT	NA	K	CHL	CAL	PHOS	MAG
1.00													
0.15	1.00												
0.11	0.36	1.00											
0.02	0.70	-0.22	1.00										
0.06	-0.32	0.51	0.88	1.00									
-0.03	0.27	0.11	0.16	-0.04	1.00								
0.05	0.19	0.05	0.11	-0.02	0.19	1.00							
-0.06	0.16	0.06	0.11	-0.03	0.83	0.37	1.00						
0.03	-0.07	0.02	-0.12	0.17	0.07	0.01	0.05	1.00					
0.07	0.01	0.06	-0.04	0.07	0.08	0.09	0.03	0.07	1.00				
-0.01	-0.10	-0.07	-0.06	0.04	0.11	-0.14	0.08	0.14	0.27	1.00			
0.08	0.44	0.33	0.17	0.04	0.15	0.14	0.08	0.14	0.19	0.07	1.00		
0.04	0.13	0.14	0.04	0.03	-0.07	0.01	-0.06	0.12	0.12	0.05	0.16	1.00	
0.19	0.21	0.13	0.10	0.01	0.16	0.16	0.05	0.15	0.32	0.10	0.22	0.01	1.00

The FACTAN program was employed to perform a factor analysis using the correlation matrix from Table 13.6 as the input (age has been substituted for service). In this example PCB serum and body burden values as Arococlor 1242 and 1260 have been incorporated. Nine factors were identified from the rotated factor loadings. The variables associated with each factor are boxed. It is apparent that the various measures of PCBs are collinear.

In Table 13.7 the variable list has been reduced. Only serum total PCBs (sum of Aroclor 1242 and 1260) is used. The A/G and the BUN/creatinine ratios have been removed. Seven factors are identified: Factor 1 associates PCBs, triglycerides and cholesterol; Factor 2 involves primarily the liver enzymes. Separate factors are identified for bilirubin, nonprotein nitrogen, blood sugar and albumin. Total protein and globulin are most strongly associated with the liver enzymes. Sex and percent body fat are interrelated.

Regression Analysis

Based on these and other studies the following approach was adopted for the regression analysis:

a. We selected measures of PCB level, sex, service and percent body fat as independent variables. Regressions were performed on each dependent variable using a single estimate of PCB level, either serum, adipose tissue or body burden, as A-1242, A-1260 or as total PCBs. In addition, levels of p, p' - DDE were used in the same manner either singly or in combination with a measure of PCB levels.

TABLE 13.6. ROTATED FACTOR LOADINGS

Table 13.6. Rotated factor loadings from FACTAN analysis. The loadings for the nine factors identified have been reordered and boxed for clarity. The factor numbering is arbitrary.

	FACTOR NUMBER								
	1	2	3	4	5	6	7	8	9
LBB42	0.95	0.14	−0.05	−0.01	−0.01	−0.04	−0.09	0.04	0.09
L1242	0.93	0.04	−0.01	0.01	−0.05	−0.21	−0.04	−0.01	−0.36
LBB60	0.82	0.04	−0.06	0.17	0.15	0.01	0.26	0.11	−0.28
L1260	0.78	−0.07	0.01	0.18	0.13	−0.19	0.30	0.06	0.08
% FAT	0.35	0.21	−0.33	0.05	0.11	0.15	−0.34	0.50	−0.20
AGE	0.27	−0.08	−0.38	0.11	0.14	0.09	0.22	0.33	−0.58
CHOL	0.23	−0.10	−0.20	[illegible]	−0.13	−0.43	0.19	0.39	−0.18
LTRI	0.21	−0.01	0.02	0.0[illegible]	−0.06	−0.79	0.01	0.28	−0.13
LGGTP	0.16	0.43	−0.10	−0.02	−0.28	−0.50	0.25	−0.04	−0.23
LSGPT	0.08	0.83	−0.01	0.15	0.01	−0.13	0.06	0.10	−0.15
LSGOT	0.03	0.86	−0.03	−0.05	−0.06	−0.05	0.09	0.06	−0.09
URIC	0.03	0.55	0.14	0.19	−0.27	−0.27	0.37	0.09	0.08
TPRO	0.01	0.52	−0.13	0.16	−0.07	−0.60	−0.05	−0.10	0.19
GLOB	0.06	0.35	−0.70	0.03	0.09	−0.54	−0.06	−0.14	0.02
ALB	−0.01	0.24	0.74	0.03	−0.06	−0.24	−0.03	−0.12	−0.07
A/GR	−0.03	−0.15	0.86	0.11	−0.12	0.33	−0.01	0.10	0.06
LBUN	0.13	0.17	0.02	0.93	0.01	−0.01	0.20	0.02	−0.07
LB/C	0.06	0.02	0.08	0.95	0.03	−0.02	−0.25	0.02	−0.06
LTBIL	−0.08	0.12	0.14	−0.04	−0.90	−0.06	0.10	0.07	0.08
DBIL	−0.04	0.04	0.06	0.01	−0.93	0.10	−0.07	−0.08	0.05
LBLS	0.04	0.13	0.11	0.08	0.07	−0.13	−0.10	−0.18	−0.86
ALK	0.05	0.15	−0.03	−0.10	0.15	−0.66	−0.02	0.05	−0.01
LDH	0.01	0.14	0.12	−0.01	−0.01	−0.24	−0.03	0.79	0.17
CRE	0.15	0.27	−0.04	−0.06	−0.01	0.02	0.86	−0.06	0.01

TABLE 13.7. ROTATED LOADING FACTORS

Table 13.7. Rotating factor loadings from FACTAN analysis. Correlation matrix has been reduced by elimination of all but one measure of PCB level, the A/G and the BUN/Creatinine ratios. Seven factors were identified.

	FACTOR NUMBER						
	1	2	3	4	5	6	7
L(Serum PCB)	0.62	0.02	−0.17	−0.03	−0.20	0.03	−0.02
LTR1	0.80	0.24	0.08	−0.06	0.10	0.11	0.04
CHOL	0.75	0.09	−0.16	0.08	−0.20	−0.13	−0.04
LGGTP	0.41	0.59	0.24	0.21	−0.10	−0.08	−0.20
LALK	0.41	0.40	0.33	−0.23	0.35	0.01	0.16
SERVICE	0.37	−0.10	−0.03	−0.17	0.51	−0.21	−0.38
LDH	0.33	0.12	−0.23	−0.01	−0.08	0.34	0.56
GLOB	0.30	0.67	−0.11	−0.17	0.19	−0.37	0.01
TPROT	0.26	0.73	−0.02	0.04	0.11	0.21	0.13
LSGOT	−0.11	0.79	−0.07	0.05	−0.20	0.06	−0.06
LSGPT	0.03	0.76	−0.05	0.08	−0.30	0.11	−0.05
URIC	0.15	0.58	0.28	0.22	−0.39	0.20	0.14
SEX	0.02	−0.12	−0.89	−0.13	0.24	0.05	0.06
% FAT	0.22	0.17	−0.79	−0.12	−0.08	−0.14	0.03
LTBIL	0.05	0.13	0.17	0.87	−0.03	0.11	0.18
DBIL	−0.06	0.03	0.05	0.93	0.08	0.01	−0.03
LBUN	0.19	0.13	−0.03	−0.02	−0.59	0.18	−0.09
CRE	−0.02	0.25	0.26	−0.02	−0.67	−0.14	0.16
LBLS	0.15	0.12	−0.04	−0.12	−0.06	0.26	−0.79
ALB	−0.01	0.14	0.17	0.08	−0.01	0.86	0.08

b. Triglycerides were used as a dependent variable either deleting the data cases with > 400 mgms/DL or using the results of the maximum likelihood technique for censored data. In the latter case the program did not provide F-ratios and other statistics of the fit. A spread factor (standard deviation) only was calculated.

c. Regressions were performed as a total regression and then checked using the backward stepwise procedure. The residuals were evaluated in each case for normality. Partial residuals were obtained when the maximum likelihood technique was used. These plots are helpful in testing the assumption of a linear model. The positions of the censored data in the plots were also examined. They were found to be randomly distributed.

Results

The results of these analyses are presented in Tables 13.8 - 13.15. The entries in the tables are the coefficients of the regression equations and the stars indicate statistical significance of the independent variable equal to or greater than 95 percent, i.e., the 95 percent confidence limits of the coefficient did not include zero.

The data may be summarized as follows.

Serum Triglycerides

There was a significant positive association between log serum triglycerides and log serum PCB levels either as Aroclor 1242, Aroclor 1260 or total PCB (Table 13.8). Equivalent relations were found using either the maximum likelihood technique or with deletion of data cases with

TABLE 13.8. TRIGLYCERIDES VS. SERUM PCB OR DDE

Table 13.8. Multiple linear regression study of serum triglycerides as dependent variable. Independent variables: serum PCB as total PCBs (Aroclor 1242 + 1260), L-PCBs and H-PCBs: serum p, p'-DDE; percent body fat, sex and service. Two cases are shown: the maximum likelihood estimate of serum triglycerides (MLE) and the case where triglyceride values ⩾400 mgms/100 ml are deleted (DELETED). The coefficients of the regression are given: stars indicate a significance at the 5 percent level or better. Using the maximum likelihood estimate the conventional statistics of the fitted equation cannot be calculated: a spread factor only is obtained (entered under S.D.).

	N	COEFFICIENTS					STATISTICS OF FIT			
TOTAL PCB's		INTERCEPT	PCB/DDE	% FAT	SEX	SERVICE	F-RATIO	SD	R	R^2
MLE*	131	1.66	0.168*	0.013*	−0.219*	−0.002	–	0.213	–	–
DELETED**	120	1.68	0.155*	0.008	−0.133*	−0.0008	6.29	0.188	0.424	0.180
L-PCB										
MLE	156	1.67	0.156*	0.014*	−0.224*	−0.001	–	0.207	–	–
DELETED	143	1.68	0.146*	0.010*	−0.144*	−0.0005	8.30	0.182	0.440	0.194
H-PCB										
MLE	126	1.80	0.222*	0.012*	−0.156*	−0.007*	–	0.208	–	–
DELETED	120	1.79	0.197*	0.008	−0.096	−0.003	6.39	0.188	0.426	0.182
DDE										
MLE	156	1.78	0.287*	0.013*	−0.197*	−0.002	–	0.203	–	
DELETED	143	1.83	0.194*	0.010*	−0.138*	−0.0007	6.46	0.186	0.397	0.158

* MLE = Maximum Likelihood Estimate
** TRIGLYCERIDES >400 mgm/100 ml deleted

> 400 mgms/100 ml, except for the correlation with percent body fat in the case of log total PCBs and log A-1260 which fell below the 95 percent significance. An equivalent association was found with p, p' - DDE. The largest F-ratio was found with log A-1242.

When PCB and DDE levels were stated as distributed in serum lipids (sum of triglycerides and cholesterol) the log serum triglyceride level was not significantly dependent on log serum PCBs or DDE (Table 13.9) but was associated with the percent body fat. When PCBs and DDE were stated as body burden (Table 13.10) log serum triglyceride level was significantly dependent only when the percent body fat was removed as an independent variable in the case of the Aroclor 1242. There was no association of log serum triglycerides and log p, p' - DDE body burden.

In Table 13.11 we show the results obtained when both PCBs and DDE are included as independent variables and compare the maximum likelihood estimates for the total population to that for males alone, and the results of the backward stepwise regression where the serum triglyceride data cases involving > 400 mgms/100 ml were deleted. For serum levels triglycerides are significantly dependent on both PCBs and DDE. Log serum triglycerides were dependent on log PCB body burden only when percent body fat was removed from the regression.

Log serum triglycerides were positively related to percent body fat but negatively related to sex, the latter arising because of the computer coding where a negative relation indicates a relation with males.

TABLE 13.9 TRIGLYCERIDES VS. ADIPOSE TISSUE PCB OR DDE

Table 13.9. Same as Table 13.8 except calculated values for adipose tissue PCBs and p, p'-DDE have been used. No significant association between serum triglycerides and adipose tissue values were found.

	N	COEFFICIENTS					STATISTICS OF FIT			
TOTAL PCB's		INTERCEPT	PCB/DDE	% FAT	SEX	SERVICE	F=RATIO	SD	R	R^2
MLE	131	1.92	0.030	0.016*	−0.222*	0.003		0.226		
DELETED	120	1.87	0.061	0.011*	−0.138*	0.0004	2.58	0.199	0.287	0.082
L-PCB										
MLE	156	1.89	0.037	0.017*	−0.232*	−0.0006		0.218		
DELETED	143	1.85	0.063	0.011*	−0.152*	−0.00004	3.92	0.192	0.319	0.102
H-PCB										
MLE	126	1.98	0.020	0.015*	−0.199*	−0.001		0.223		
DELETED	120	1.94	0.043	0.011*	−0.129*	−0.0002	2.22	0.200	0.268	0.072
DDE										
MLE	156	1.94	−0.012	0.018*	−0.229*	−0.0004		0.219		
DELETED	143	1.94	−0.044	0.014*	−0.150	0.0004	3.29	0.194	0.295	0.087

TABLE 13.10 TRIGLYCERIDES VS. PSC OR DDE BODY BURDEN

Table 13.10. Same as Table 13.8 except calculated values for PCB and p, p'-DDE body burden have been used. When percent body fat is eliminated as an independent variable, an association was found between the L-PCB body burden and the serum triglycerides.

	N	COEFFICIENTS					STATISTICS OF FIT			
TOTAL PCB's		INTERCEPT	PCB/DDE	% FAT	SEX	SERVICE	F=RATIO	SD	R	R^2
MLE $\bar{c}$ FAT*	131	1.98	0.030	0.015*	−0.214*	−0.0002		0.226		
$\bar{s}$ FAT**	131	2.22	0.083	–	−0.093	0.001		0.233		
DEL $\bar{c}$ FAT	120	2.01	0.064	0.008	−0.121	0.0005	2.64	0.199	0.290	0.084
$\bar{s}$ FAT	120	2.14	0.094*	–	−0.051	0.001	2.49	0.200	0.246	0.060
L-PCB										
MLE $\bar{c}$ FAT	156	1.97	0.037	0.016*	−0.222*	−0.0005		0.218		
$\bar{s}$ FAT	156	2.23	0.094*	–	−0.094*	0.001		0.226		
DEL $\bar{c}$ FAT	143	2.00	0.066	0.010*	−0.135*	0.0002	3.97	0.192	0.321	0.010
$\bar{s}$ FAT	143	2.14	0.101*	–	−0.053	0.001	3.54	0.195	0.266	0.070
H-PCB										
MLE $\bar{c}$ FAT	126	2.03	0.023	0.014*	−0.192*	−0.001		0.233		
$\bar{s}$ FAT	126	2.32	0.093	–	−0.066	−0.001		0.228		
DEL $\bar{c}$ FAT	120	2.05	0.049	0.009	−0.115	−0.0003	2.27	0.200	0.271	0.073
$\bar{s}$ FAT	120	2.24	0.097	–	−0.031	−0.0003	1.90	0.202	0.261	0.047
DDE										
MLE $\bar{c}$ FAT	156	1.91	−0.013	0.018*	−0.233*	−0.0004		0.219		
$\bar{s}$ FAT	156	2.37	0.112	–	−0.085	0.001		0.228		
DEL $\bar{s}$ FAT	143	2.21	0.056	–	−0.038	0.002	1.03	0.200	0.48	0.218

* % Body fat included as independent variable
** % Body fat removed as independent variable

TABLE 13.11. TRIGLYCERIDES VS TOTAL PCB's AND DDE

Table 13.11. Same as Table 13.8 except PCB's and p, p'-DDE both included as independent variables and male data has been analyzed separately. Backward step regrssion (DELSTEP) showed a PCB body burden and serum triglyceride association only upon deletion of percent body fat as an independent variable.

	N	INTERCEPT	PCB	DDE	%FAT	SEX	SERVICE	F-RATIO	SD	R	R^2
			COEFFICIENTS						STATISTICS		
SERUM											
MLE	131	1.57	0.131*	0.257*	0.009	−0.176*	−0.002		0.201	–	–
MLE, MALES	105	1.35	0.153*	0.236*	0.009	–	−0.001		0.216		
DEL. STEP	125	1.56	0.139*	0.222*	–	–	–	19.60	0.186	0.493	0.243
ADIPOSE											
MLE	131	1.92	0.032	−0.032	0.017*	−0.824*	−0.0003		0.226		
MLE, MALES	105	1.60	0.062	−0.111	0.018*	–	0.0009		0.239		
DEL. STEP	125	1.94	–	–	0.014*	−0.169*	–	5.90	0.204	0.297	0.088
BODY BURDEN											
MLE c̄ FAT	131	1.92	0.032	−0.031	0.016*	−0.224*	−0.0003		0.226		
s̄ FAT	131	2.32	0.068	0.072	–	−0.095	0.001		0.233		
MLE, MALES											
c̄ FAT	105	1.49	0.062	−0.106	0.020*	–	0.0008		0.239		
DEL STEP											
c̄ FAT	125	1.94	–	–	0.014*	−0.169*	–	5.90	0.204	0.297	0.088
s̄ FAT	125	2.10	0.102*	–	–	–	–	6.38	0.208	0.222	0.043

Other Variables

Serum cholesterol has a positive significant association with log serum PCBs and LDDE but not when stated as adipose tissue or body burden. Serum cholesterol was service- and/or age-dependent. Log serum GGTP is associated with log serum total PCBs, primarily the Aroclor-1242 component, but not with log serum DDE. These same associations were found with body burden values (when percent fat is omitted in the regression) but not with adipose tissue levels where the association was with percent body fat.

Table 13.12 is equivalent to Table 13.11 where both PCB and DDE are independent variables and males are analysed separately. In the backward stepwise regressions log serum GGTP was shown to be associated with percent body fat rather than PCBs when fat is included as an independent variable.

In Tables 13.13-13.15 a positive coefficient for sex was found in the case of LDH but the regression equation was not significant. A positive relation was also found in the case of Aro-1260, DDE body burden and cholesterol which were statistically significant.

Log serum SGOT and direct bilirubin were negatively but not significantly related to log serum total PCBs, but these relations disappeared for log PCB body burden. A number of variables were significantly related to body fat in the adipose tissue regression (Table 13.13): namely, the liver enzymes (GGTP, SGOT and SGPT), serum proteins (total protein, globulin) and nonprotein nitrogen constituents (BUN, creatinine and uric acid).

TABLE 13. 12 TOTAL PCBs AND DDE

Table 13.12 Same as Table 13.8 except PCBs and p,p'-DDE both included as independent variables and male data has been analyzed separately. Backward step regression (STEPALL) showed a PCB body burden and serum GGTP association only upon deletion of percent body fat as an independent variable.

	N	COEFFICIENTS						STATISTICS OF FIT			
SERUM		INTERCEPT	PCB	DDE	%FAT	SEX	SERVICE	F-RATIO	SD	R	R^2
CHOLESTEROL	131	106.67	24.82*	40.54*	0.761	−10.32	1.31*	8.07	45.66	0.494	0.244*
MALE	105	103.75	23.66*	47.94*	0.177	.	1.51*	9.21	47.81	0.519	0.269*
STEPALL	131	110.51	25.02*	43.23*	.	.	1.42	13.37	45.43	0.490	0.240*
LGGGTP	131	0.917	0.099	0.107	0.009	−0.287*	0.0007	5.91	0.243	0.437	0.191*
STEPALL	131	0.959	0.177*	.	0.011	−0.308	.	9.17	0.243	0.422	0.179*
ADIPOSE											
CHOLESTEROL	131	170.01	5.89	−14.34	2.12	−18.36	1.60*	3.93	48.82	0.369	0.136
MALE	105	149.55	7.14	−15.45	1.96	.	1.86*	4.46	51.52	0.389	0.152*
STEPALL	131	206.16	.	.	.	.	1.98	14.98	48.94	0.323	0.104*
LGGTP	131	1.06	0.071	0.018	0.012*	−0.310*	0.001	4.61	0.248	0.395	0.156*
STEPALL	131	1.17	.	.	0.014*	−0.317*	.	10.34	0.248	0.373	0.139*
BODY BURDEN											
CHOLESTEROL											
c̄ FAT	131	149.20	5.59	−15.11	2.44	−20.79	1.58*	3.95	48.81	0.369	0.137*
MALE	105	128.53	7.10	−15.53	2.24	.	1.84*	4.47	51.52	0.389	0.152*
STEPALL	131	206.16	.	.	.	.	1.98	14.98	48.94	0.323	0.104*
s̄ FAT	131	208.39	10.93	0.181	.	−1.66	1.83*	4.01	49.27	0.336	0.113*
MALE	105	202.01	10.84	0.171	.	.	2.11*	5.23	51.78	0.368	0.134*
STEPALL	131	206.16	.	.	.	.	1.98	14.98	48.94	0.323	0.104*
LGGTP											
c̄ FAT	131	1.24	0.068	0.101	0.010	−0.291*	0.002	4.57	0.249	0.393	0.155*
STEP	131	1.17	.	.	0.014*	−0.317*	.	10.34	0.248	0.373	0.139*
s̄ FAT	131	1.47	0.089	0.071	.	−0.215*	0.003	5.15	0.250	0.375	0.140*
STEP	131	1.43	0.116*	.	.	0.218*	.	9.34	0.250	0.357	0.127*

TABLE 13.13 SERUM LEVELS

Table 13.13 Multiple linear regression study of other biochemical serum variables, each taken singly as the dependent variable. Independent variables are serum PCBs (total), percent body fat, sex and service. Serum cholesterol and log GGTP were analyzed with serum L-PCB, H-PCB, and p, p'-DDE. The table entries are the same as Table 13.8-11. A number of significant regressions were observed not involving PCBs which have been starred.

	N	COEFFICIENTS					STATISTICS			
		INTERCEPT	SERUM TPCB	%FAT	SEX	SERVICE	F-RATIO	SD	R	R^2
CHOLESTEROL	131	120.76	30.62*	1.47	−17.00	1.29*	7.67	46.92	0.442	0.196*
LGGTP	131	0.954	0.115*	0.011*	−0.304*	0.0007	6.84	0.244	0.422	0.178*
LSGOT	130	1.39	−0.001	0.006*	−0.095*	−0.0008	1.51	0.138	0.214	0.046
LSGPT	130	1.42	0.024	0.010*	−0.177*	−0.002	4.26	0.152	0.346	0.120*
LDH	131	136.23	2.25	1.00	4.58	−0.112	1.52	32.39	0.214	0.046
LALKPH	131	1.36	0.0[illegible]2	0.003	−0.035	−0.002	1.45	0.112	0.210	0.044
LTBIL	131	−0.073	0.013	0.003	−0.157*	−0.004*	4.84	0.157	0.365	0.133*
LDBIL	131	−0.693	−0.006	−0.001	−0.088	−0.004	1.69	0.240	0.226	0.059
TPRO	131	6.87	0.134	0.018	−0.224	−0.009	2.20	0.418	0.255	0.065
ALB	131	4.80	0.092	−0.119*	−0.009	−0.004	2.67	0.380	0.280	0.078
GLOB	131	2.17	0.097	0.023*	−0.142	−0.0005	3.23	0.382	0.305	0.098
LBUN	131	1.11	0.0[illegible]	0.007*	−0.105*	0.0008	4.31	0.107	0.347	0.120*
CRE	131	1.29	[illegible]	0.008*	−0.209*	0.001	4.60	0.184	0.357	0.128*
URIC	131	56.60	1.90	1.21*	−26.06*	−0.225	20.18	10.00	0.625	0.391*
LBLS	131	1.96	0.0003	0.001	−0.024	0.001*	2.63	0.051	0.278	0.071
			SERUM L-PCB							
CHOLEST	156	129.76	27.04*	1.45	−15.22	1.27	8.35	45.60	0.426	0.181
LGGTP	156	1.01	0.115*	0.012*	−0.336*	−0.001	9.37	0.241	0.446	0.199
			SERUM H-PCB							
CHOLEST	131	136.48	45.62*	1.92	−7.37	0.349	9.13	46.06	0.474	0.225
LGGTP	131	1.08	0.098	0.011*	−0.283*	−0.0007	5.99	0.247	0.400	0.160
			SERUM DDE							
CHOLEST	156	155.97	37.39*	1.39	−11.84	1.28*	7.65	45.95	0.411	0.169
LGGTP	156	1.18	0.056	0.013*	−0.334*	0.0008	7.43	0.246	0.406	0.165

TABLE 13.14 ADIPOSE TISSUE LEVEL

Table 13.14 Same as Table 13.13 except calculated adipose tissue PCBs and p, p'-DDE have been used. There were no significant associations with PCBs of p, p'-DDE.

	N	COEFFICIENTS					STATISTICS OF FIT			
		INTERCEPT	ADIPOSE TPCB	%FAT	SEX	SERVICE	F-RATIO	SD	R	R^2
CHOLESTEROL	131	168.31	5.01	1.97	−17.41	1.62*	4.74	48.78	0.362	0.131*
LGGTP	131	1.06	0.072	0.012*	−0.312*	0.001	5.80	0.247	0.394	0.156*
LSGOT	130	1.40	−0.003	0.006*	−0.095*	−0.0005	1.51	0.138	0.215	0.046
LSGPT	130	1.45	0.009	0.011*	−0.177*	−0.002	4.10	0.152	0.340	0.116*
LDH	131	141.18	−0.687	1.05	4.67	−0.076	1.49	32.40	0.212	0.045
LALKPH	131	1.41	0.021	0.003	−0.037	−0.001	0.766	0.113	0.154	0.024
LTBIL	131	−0.051	0.0008	0.003	−0.157*	−0.004*	4.80	0.157	0.363	0.132*
LDBIL	131	−0.715	0.009	−0.001	−0.089	−0.005	1.69	0.240	0.226	0.050
TPRO	131	7.07	0.028	0.02*	−0.226	−0.008	1.56	0.422	0.217	0.047
ALB	131	4.95	0.083	−0.018	0.017	−0.003	2.57	0.380	0.274	0.075
GLOB	131	2.32	0.016	0.025*	−0.143	0.0006	2.81	0.384	0.286	0.082
LBUN	131	1.13	0.010	0.007*	−0.106*	0.0009	4.13	0.107	0.341	0.116*
CRE	131	1.27	0.028	0.008*	−0.212*	0.001	4.71	0.184	0.361	0.130*
URIC	131	59.22	0.559	1.24*	−26.06*	−0.225*	20.18	10.00	0.625	0.391*
LBLS	131	1.97	−0.006	0.001	−0.023	0.001	2.70	0.051	0.281	0.079
			ADIPOSE L-PCB							
CHOLEST	156	169.45	4.92	2.02*	−16.47	1.42*	5.31	47.18	0.351	0.123*
LGGTP	156	1.11	0.076	0.013*	−0.346*	−0.001	8.04	0.244	0.491	0.175*
			ADIPOSE H-PCB							
CHOLEST	131	172.72	6.04	1.97	−16.24	1.51*	4.73	48.73	0.361	0.181*
LGGTP	131	1.15	0.023	0.013*	−0.304*	0.001	5.30	0.249	0.379	0.144*
			ADIPOSE DDE							
CHOLEST	156	178.23	−20.26*	2.27*	−16.22	1.51*	5.82	46.90	0.365	0.134
LGGTP	156	1.22	−0.069	0.015*	−0.340*	−0.0004	7.49	0.246	0.407	0.166*

TABL[illegible]5 BODY BURDEN VALUES

Table 13.15 Same as Table 13.13 except calculated values for PCB and p, p'-DDE body burden have been used. Log GGTP is associated with L PCB when percent body fat is removed as an independent variable.

	N	COEFFICIENTS					STATISTICS OF FIT			
		INTERCEPT	BURDEN TPCB	%FAT	SEX	SERVICE	F-RATIO	SD	R	R^2
CHOLESTEROL	131	208.14	10.97	.	−1.65	1.83*	5.39	49.08	0.336	0.113*
LGGTP	131	1.38	0.103*	.	−0.213	0.003	6.54	0.250	0.366	0.134*
LSGOT	130	1.49	0.018	.	−0.0[illegible]3	−0.0001	0.730	0.139	0.131	0.017
LSGPT	130	1.63	0.047	.	−0.091*	−0.0005	2.56	0.157	0.240	0.057
LDH	131	156.53	2.97	.	13.06	0.034	1.30	32.53	0.173	0.030
LALKPHO	131	1.49	0.029	.	−0.012	−0.001	0.718	0.113	0.129	0.017
LTBIL	131	−0.003	0.012	.	−0.133*	−0.004*	6.19	0.156	0.357	0.128*
LDBIL	131	−0.721	0.004	.	−0.100	−0.005	3.24	0.239	0.224	0.050
TPRO	131	7.44	0.099	.	−0.066	−0.006	0.822	0.427	0.138	0.019
ALB	131	4.72	0.014	.	−0.159	−0.005	1.61	0.387	0.191	0.037
GLOB	131	2.74	0.097	.	−0.057	0.003	1.16	0.394	0.163	0.027
LBUN	131	1.26	0.031	.	−0.051*	0.002	3.02	0.109	0.258	0.067
CRE	131	1.44	0.051	.	−0.148*	0.002	5.26	0.185	0.333	0.111*
URIC	131	79.7[illegible]	4.24*	.	−16.16	−0.097	14.75	10.99	0.508	0.258*
			BURDEN L-PCB							
CHOLEST	156	210.06	11.12	.	−0.379	[illegible]65*	5.84	47.56	0.321	0.103*
LGGTP	156	1.45	0.11[illegible]	.	−0.241	0.004	9.07	0.247	0.390	0.152*
			BURDEN H-PCB							
CHOLEST	131	223.17	14.68	.	−0.907	1.54*	5.47	49.04	0.338	0.114*
LGGTP	131	1.19	0.08	.	−0.189*	0.002	5.53	0.252	0.340	0.116*
			BURDEN DDE							
CHOLEST	156	205.59	−1.23	.	2.19	1.75*	5.17	47.84	0.304	0.093*
LGGTP	156	1.49	0.04	.	−0.220*	0.001	6.66	0.252	0.341	0.116*

Discussion

In classic Yusho (PCB+PCDF+PCQ) poisoning the predominant biochemical finding has been an elevation in serum triglyceride level. This has been interpreted in the Japanese literature to be a consequence of a lowered triglyceride removal through diminished lipoprotein lipose activity at the tissue level. Normal levels of cholesterol were found. Although pathological evidence for the induction of mixed function oxidase was determined in one subject, no abnormalities of serum GOT, GPT or BSP retention were found. Alkaline phosphatose and α_2 - globulin levels were slightly elevated, serum albumin and total bilirubin decreased. The principal evidence for induction of mixed function oxidase activity was indirect and consisted of hormone degradation and endocrine disorders.[19]

In Aroclor 1242 exposure associated with capacitor manufacture, Ouw et al.[20] found some individual abnormal results (elevated total protein, decreased α_1 - globulin, elevated GPT) but the population means were within the normal range. In the Fischbein et al. study[21] of 32 workers exposed sequentially to Aroclor 1254, 1242 and 1016 there was also a paucity of abnormal results. Cholesterol values were elevated in 17.8 percent (>300 mgms/100 ml) but only 5.4 percent of the population showed triglyceride values >250 mgms/100 ml. BUN and creatinine levels

19 PCB Poisoning and Pollution, E.K. Higuchi, Academic Press, New York 1976.

20 Ouw, K.H., Simpson, G.R., and D.S. Siyali. The Use and Health Effects of Aroclor 1242, A Polychlorinated Biphenyl in an Electrical Industry. Arch. Env. Health 32: 189-194, 1976.

21 Fischbein, A., Wolff, M.S., Lilis, R., Thornton, J., and I.J. Selikoff. Clinical Findings Among PCB-Exposed Capacitor Manufacturing Workers. Ann. N.Y. Acad. Sci. 320: 703-715, 1979.

were increased in 5.5 and 4.0 percent respectively, but only six subjects showed elevated levels of SGOT, SGPT and LDH and none were elevated in the case of alkaline phosphatase and bilirubin.

Maroni et al.(22) studied 80 capacitor workers exposed to Piralone 3010 and Apirolio, both containing 42% chlorine, and found more or less pronounced hepatic involvement with hepatomegaly in some and increases in serum GGT, AST (aspartate aminotransferase), ALT (alanine aminotransferase) and OCT (orthithin - carbamayl transferase). None of the workers had a history of ''excessive'' intake of alcohol or drugs. There was a statistically significant association between the prevalence of liver involvement and blood PCB level which was more pronounced for the lower homologs.

Recently two papers have appeared in which the relation of xenobiotics to the biochemical variables in blood were studied by multiple linear regression techniques. Kreiss et al.(23)(24) studied a group of 500 subjects exposed to DDT (mostly) and PCBs (assayed as Aroclor 1260), presumably from a common dietary source. Serum DDT and PCB levels were strongly correlated (R = 0.83) and both were a function of age. Serum cholesterol, but not triglyceride level was a significant independent predictor of serum PCB level, but no relation was found with HDLC. Log γ-glutamyl transpeptidase was positively correlated with log serum PCB

22 Maroni, M., Columbi, A., Arbosti, G. et al. Occupational exposure to polychlorinated biphenyls in electrical workers. II. Health effects. Brit. J. Ind. Med. 38: 55-60, 1981.

23 Kreiss, K., Zack, M.M., Kimbrough, R.D. et al., Cross-sectional Study of A Community with Exceptional Exposure to DDT., JAMA 245: 1926-1930, 1981.

24 Kreiss, K., Zack, M.M., Kimbrough, R.D. et al., Association of Blood Pressure and Polychlorinated Biphenyl Levels, JAMA 245: 2505-2509, 1981.

independent of alcohol consumption and age, but other liver function tests (total bilirubin, serum glutamic pyruvic transaminase) were not correlated. Log serum PCBs were a negative function of the body mass index.

Log serum DDT was positively correlated with log serum triglycerides, with serum cholesterol and with log GGT, but no correlation was found with obesity independent of triglycerides, cholesterol and age. The analysis was complicated by the collinearity of DDT and PCBs and of triglycerides and cholesterol. The retention of DDT with age was not associated with urinary findings, serum creatinine or history of kidney disease. The DDT isomers, o,p' - and p,p' - DDE, made up 86.7 percent of the total DDT level.

In a study by Smith et al.[25] three groups of workers occupationally exposed to PCBs were analyzed with respect to job exposure and health effects. The population included 231 capacitor workers exposed to Aroclor 1242 and 1016 (but not Aroclor 1254) and 93 transformer maintenance and repair employees exposed to Aroclor 1254. PCBs were quantitated as lower and higher homologs using Aroclor 1242 and 1254. Standard peaks with equivalent retention times were quantitated only once by using peaks before DDE as lower homologs and those after as higher homologs. In multiple linear regression studies the coefficients for the higher and lower homologs were remarkably similar suggesting similar absorption and metabolism kinetics. A statistical test of the equality of the regression coefficients showed them to be

25 Smith, A.B., Schloemer, J., Lowry, L.K., et al. Metabolic and Health Consequences of Occupational Exposure to Polychlorinated Biphenyls (PCBs). NIOSH report, April 1981, (to be published).

indistinguishable for age, sex and duration of exposure, but different for job classification. This led to the finding that the serum H-PCB was a function of present job category and not a measure of cumulative exposure.

This finding is at variance with the present study where there was substantial exposure to Aroclor 1254 and to the findings of Maroni et al. where the higher homologs were found in greater concentration than the lower homologs and were correlated with the duration of exposure.

Smith et al. found significant partial correlations, in the presence of confounding variables, between log (SGOT), log GGTP, cholesterol and log (triglyceride) and either serum log (L-PCB) or log (H-PCB) levels at at least one site, but the trend was not homogeneous for cholesterol across all three sites. Log HDL-cholesterol was negatively correlated with log (H-PCB).

The positive relation of serum lipids and serum PCBs which we report, and which has been found by others, appears to be adequately explained by the fact that PCBs tend to distribute equally among all nonstructural lipid compartments in the body, and hence PCB levels in the serum must, of necessity, follow those of the serum lipids. The generality of the phenomenon is further demonstrated by the equivalent association between p, p' - DEE and serum lipids in this population. Serum lipoproteins were not determined so that the relative importance of the various individual serum lipid compartments involved is uncertain. Smith et al. reported a negative association of serum PCBs and

HDL-cholesterol (not confirmed by Kreiss et al.). However, in our study the cholesterol to triglyceride ratio declined as their sum increased (Figure 13.21 suggesting a declining HDL-cholesterol level with an increasing pre-Beta and Beta-lipoprotein fraction as the total lipids increased.

This analysis indicates the importance of percent body fat as a regressor variable. In the Kreiss et al. study they observed a negative correlation of obesity (as measured by the body mass index) with serum PCB level in their subjects with relatively low serum PCB levels. In our highly exposed subjects the relation was positive; that is, the larger the lipid reservoir, the higher the body burden. The effects of changes in body weight on serum PCB levels are well documented. Following weight loss, higher serum PCB levels are observed.[23,24,25,26] We have had an opportunity to observe one case of hypertriglyceridemia in which a nonfat vegetable diet reduced the level from 675 to 218 mgms/100 ml which was associated with a reduction of serum Aroclor 1242 levels from 1195 to 774 ppb in approximately one month.

The association of hypertriglyceridemia and obesity has been studied by Albrink and Meigs[27] in an industrial population in which as many as 40 percent of the males were observed to have elevated serum triglycerides. They differentiated ''acquired'' adult obesity from "natural" lifelong obesity by skinfold thickness measurements and

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26 Hesselberg, R.J. and D.D. Sherr, PCB's and p,p'-DDE in the blood of cachetic patients. Bull. Environ. Contam: Topical. <u>11</u>: 202-205, 1974.

27 Albrink, M.J. and J.W. Meigs, Interrelationship Between Skinfold Thickness, Serum Lipids and Blood Sugar in Normal Men, Am. J. Clin. Nutrition, <u>15</u>: 255, 1964

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7395B C1  07-21-81   14.977   GE-CRD TSS MEDIA CONVERSION

LINE       CONTENTS                                FNAME - CH-TRI

CROSSPLOT (CHTRI; LIP79)

    CHTRI       LIP79  CELL LOWER ENDPT
NO. CELL
IN  LOWER      120.00    320.00    520.00    720.00
ROW ENDPT           220.00    420.00    620.00
               <+....+....+....+....+....+....+..>
        ABOVE
        5.0000+
  1     4.8000+           1
        4.6000+
        4.4000+
        4.2000+
        4.0000+
  1     3.8000+         1
        3.6000+
  4     3.4000+          22
  3     3.2000+          1 11
  2     3.0000+          1     1
  4     2.8000+       1 1  1    1
  3     2.6000+          1 2
 13     2.4000+       113 223    1
 18     2.2000+       12 1241311 1  1
 13     2.0000+       11112311 2
 10     1.8000+        13 21 1    1   1
 28     1.6000+  1    11111245115121
 15     1.4000+          1111211122 1      1
 17     1.2000+          1  12421121   1  1
 15     1.0000+           2 3 22 111      1 2
 12     0.8000+                11     111 2  11 1 1
 12     0.6000+                 1   1   1  2223
  3     0.4000+                        21
        BELOW+
               <+....+....+....+....+....+....+..>
       NO.              10  15    9   4   3   5
       IN        1       10  14    7            3   1
       COL.           5   15  9   8   2   4    3
                       6   17  12  3   4   3    1  174 TOTAL

  20 CASES WITH MISSING VALUES OMITTED FROM THE ABOVE.

14.963 O'CLOCK; PROCESSOR=   0.4 SEC; TOTAL=   16.9 SEC
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Figure 13.21. Cross-plot of the serum cholesterol to serum triglyceride ratio vs. the sum of serum triglycerides and cholesterol (LIP79). The mean value of the ratio is 1.77.

13.21

found that the triglyceride elevations were associated with acquired trunkal rather than the innate extremity obesity.

Martin, et al.[28] have described a significant positive association between serum GGTP and serum triglyceride concentration, particularly with the pre-β lipoprotien fraction in 109 consecutive patients. They suggested that the association was due to microsomal enzyme induction by carbohydrate excess, in particularly phosphatidic acid phosphatase which converts α,β-diglyceride phosphate to α,β-diglyceride in triglyceride synthesis. These findings suggest that the correlations between the serum levels of PCBs and GGTP seen in our population could arise from the association of both of these parameters with manifestations of dietary excess.

There is now abundant evidence that many of the individual PCB isomers in the group analytically described as ''Aroclor 1242'' or as ''Lower PCBs (L-PGB)'' are capable of inducing the P450 type of mixed function oxidases in laboratory animals. A few individual isomers in the groups reported by analysts as ''Aroclor 1254,'' ''Aroclor 1260,'' or ''higher PCBs (H-PCB)'' are clearly capable of inducing the P448 type oxidases in rodents if present at sufficiently high levels. The direct measurement of either type of mixed function oxidase induction currently requires use of liver tissue samples; as a consequence they can be evaluated in human patients only through indirect measures. Such measures, e.g., manifestations of chloracnogenic response as indicators of P448 activity, currently provide no evidence that H-PCBs alone, at the

28 Martin, P.J., Martin, J.V. and D.M. Goldberg, γ-glutamyl Transpeptidase, Triglycerides and Enzyme Induction, Brit. J. Med 1: 17-18, 1975.

serum levels seen to date, have even led to P448 induction in humans. However, preliminary evidence for P450 inductions in PCB-exposed capacitor workers, as indicated by reduced antipyrine clearance times, has been reported by Alvares et al.[29]

As previously noted, the Japanese investigators of the Yusho (PCT+PCDF+PCQ) poisoning episode noted alterations in steroid metabolism which they ascribed to mixed function oxidase activation. In addition, Hirayama et al.[30] have reported hypobilirubinemia in follow-up studies in Yusho patients and ascribed the finding to mixed function oxidase induction and augmented bilirubin elimination. Both serum triglycerides and serum PCBs (H-PCBs) were significant inverse functions of serum bilirubin concentration. Neither finding was observed in our population of PCB-exposed capacitor workers, but we did note a non-significant inverse correlation between log serum Aroclor 1242 and 1260 and log direct bilirubin. It probably should also be noted that at the time of Hirayama's measurement, the PCB levels in the Yusho population had fallen to levels below that of the US background; hence their possible clinical significance is uncertain.

In summary it would appear that the simple correlations of serum PCB levels with those of serum lipids, serum enzymes such as GGTP, and serum bilirubin do not provide an adequate basis for inferring that PCBs can effect alterations in human liver functions. For our own

29 Alvanes, A.P., Fischbein, A., Anderson, K.E. and A. Kappas, Alterations in Drug Metabolism in Workers Exposed to Polychlorinated Biphenyls, Clin. Pharmacol. Therap. 22: 140-146, 1977.

30 Hirayama, C., Okumura, M, Nagai, J. and Y. Masuda, Hypobilirubinemia in Patients with Polychlorinated Biphenyl Poisoning, Clinica Chem. Acta 55: 97-100, 1974.

population, it is clearly apparent that there is no correlation between serum lipid levels and those of adipose tissue PCB, which should provide the most direct measure of the pharmacological activity of the PCB in the body. Instead, we have a correlation of serum PCB levels with those of serum liquids, which arises because of the way in which PCBs are distributed in the body and presumptivity also correlations with other parameters that are themselves also correlated with the levels of serum lipids.

At present, we regard caloric excess and consequent obesity as the primary sources of the variations in lipid metabolic patterns that have led to the serious association between PCB levels and liver function indications in the past.

According to current interpretations, caloric excess gives rise to sporadic hyperglycemia stimulating production of insulin, the most potent hormone relating to lipoprotein lipase activity. Insulin-enhanced lipase activity accelerates lipid uptake and deposition in the fat depots and induces lipolysis. Weight increases during this ''dynamic'' phase of obesity[31] accompanied by a relatively normal serum triglyceride level. With established stable adult obesity basal hyperinsulinism develops[32] associated with peripheral ''insulin resistance'' which reduces lipase activity and the serum triglycerides rises.

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31 Sims, E.A., Horton, E.S. and L.B. Salans, Inducible Metabolic Abnormalities During the Development of Obesity, 22: 235-280, 1971.

32 Rabinowitz, D., Some Endocrine and Metabolic Aspects of Obesity, Ann. Rev. Med 21: 241-258, 1970.

As for an explanation as to why our study population should be exhibiting an elevated prevalence of obesity-related effects, occurring primarily in males, we can offer no better answer at the moment than the conventional vague generalities relating to the life style of modern man - lack of exercise, too much food, and the frustrations and psychic stress of industrial life. However, studies of this population and its biochemical characteristics are continuing.

14. Pulmonary Findings

Pulmonary function has not been widely studied in association with PCB exposure. Yusho patients reported cough and sputum production suggestive of chronic bronchitis, and although PCB's were found in sputum, pulmonary function was within normal limits (19). Intravenous injection of radiolabeled PCB in mice shows selective concentration and retention in the lung (20). Certain of the isomers appeared to be retained in the bronchial mucosa because of structural specificity (21). Methylsulfonyl metabolites of some of the bronchial-seeking PCBs also accumulate, (22) suggesting PCB metabolism in the lung in mice, but these observations have not been replicated in man. In addition, pulmonary tissue activity metabolizes lipid, (23) to which PCBs are preferentially bound. For these reasons the occurrence of respiratory disease and dysfunction in PCB-exposed workers are of interest.

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19. Shigematsu, N., Ishimaru, S., Saito, R., et al., Respiratory involvement in polychlorinated biphenyl poisoning, Envir. Res. 16: 92-100, 1978.

20. Berlin, M., Gage, J., and S. Holm. The distribution and me bolism of 2,4,5,2',5'-pentachlorobiphenyl. Arch. Environ. Health 30: 141-147, 1975.

21. Brandt, I. Tissue localization of polychlorinated biphenyls: chemical structure related to pattern of distribution. Acta Pharmacol Toxicol: 40 (Suppl 11), 1977.

22. Bergman, A., Brandt, I., and B. Jansson. Accumulation of methylsulfonyl derivatives of some bronchial-seeking polychlorinated biphenyls in the respiratory tract of mice. In: Transformations of some organochlorine compounds in the environment studied by gas chromatography and mass spectrometry. Thesis. B. Jannsson. Nat. Swedish Environmental Protection Board Publication SNV PM 1037, 1978.

23. Heinemann, H.O. and A.P. Fishman. Physiol. Rev. 49: 1- , 1969.

Warshaw et al. (24) performed spirometric studies of a group of volunteer capacitor workers, some of whom had high occupational exposure to PCBs and reported a substantial prevalence of reduced vital capacity (FVC < 80 percent of predicted value). The prevalance (14 percent) was equivalent to that reported for asbestos workers. Of those showing FVC reductions, 80 percent showed a restrictive pattern without radiological changes. PCBs were not reported as an acute direct pulmonary irritant, although 8-hour time weighted average air levels in the PCB-exposed workplace varied from 0.6-11.0 mgms/m^3 (25).

In this section we summarize our spirometric studies on direct occupational exposure to PCBs in 1976 (Study Group 1). As already indicated, this group was drawn from the same plant population as that on the Warshaw et al. study but had had average PCB exposures, as judged by serum PCB levels, about eight times higher.

Methods

As noted in Section 6 above, the initial 1976 examination consisted of a medical history, physical examination, chest x-ray, ECG, an SMA-26 blood analysis, and spirometry. Body weight was obtained in light indoor clothing and height determined without shoes. In 1979 the subjects were recalled for reexamination. Chest x-ray, ECG and physical examination were repeated only in selected subjects, but special atten-

24. Warshaw, R., Fischbein, A., Thornton, J., Miller, A., and I.J. Selikoff. Decrease in vital capacity in PCB-exposed workers in a capacitor manufacturing facility. Ann. N.Y. Acad. Sci. 320: 277-283, 1979.

25. Fischbein, A., Wolff, M.S., Lilis, R., Thornton, J., and I.J. Selikoff. Clinical Findings Among PCB-Exposed Capacitor Manufacturing Workers. Ann. N.Y. Acad. Sci. 320: 703-715, 1979.

tion was given to the smoking history.

In the interim between 1976 and 1979 at [illegible] t one examination was performed on each individual in rotation, so that by 1979 most subjects had had at least two previous trials in the performance of spirometry and were relatively comfortable with the procedure.

Pulmonary function was evaluated in 1976 using a Vanguard* spirometer wit an analog output. Measurements were made in the standing position with a disposable filter sensor. The nose was closed with the fingers. Computation for FVC, FEV, and FEV_1/FVC were performed manually by measurements from tracings and a slide rule.

In 1979 measurements were made in a similar manner with a Vanguard* DS 502 spirometer with a preprogrammed computer print-out which utilized the Morris (26) standards. In interpreting the data we have followed Knudson et al (27), recalculating the data using their standards and broadening the normal range for FEV_1/FVC to >70 percent as recommended by ATS (28). The calibration source was a VS 300 3-liter volume calibrating syringe.

In both 1976 and 1979 the maximum expiratory flow curve was recorded and examined for adequacy and reproducibility of each subject's

* Life Support Engineering Corp., Woburn, MA

26. Morris, J.F., Koski, A., and L.C. Johnson. Spirometric standards for healthy non-smoking adults. Am. Rev. Resp. Dis. 103: 57-67, 1971.

27. Knudson, R.J., Slatin, R.C., Lebowitz, M.D., and B. Burrows. The maximum expiratory flow volume curve: Normal standards, variability, and effects of age. Am. Rev. Resp. Dis. 113: 587-600, 1976.

28. ATS Statement - Snowbird Workshop on standardization of spirometry. Am. Rev. Respir. Dis. 119: 832-838, 1979.

effort. At least three trials were performed by each subject and reproducibility accepted at the 10 percent level. Tracings were examined for freedom from test artifacts (29) and the highest test for FVC and FEV_1 used.

In 11 individuals for whom spirometry was not obtained in 1979, the 1976 tracings were reexamined and found acceptable, the manual calculation was repeated and these data were included in the study. In 7 individuals an acceptable test was never obtained due to dental problems, thoracic cage arthritis and other readily apparent causes.

Usable respiratory data was obtained therefore on 187 individuals (146 males and 41 females).

The parameters FVC, FEV_1 and FEV_1/FVC were found to be normally distributed. Examination of the distributions of the spirometric variables showed four individuals (3 males, 1 female) as outliers with markedly reduced respiratory function due to established chronic obstructive lung disease. These subjects were omitted in deriving the regression equations but not in the evaluation of the prevalence of pulmonary disease.

Subjects were coded for computer analysis as nonsmokers (1), ex-smokers (2) and smokers (3). Pipe and cigar smokers were coded as non-smokers. Smoking was recorded as number of packs per year, number of years smoked and the product or total packs smoked. Regression analysis showed that the coefficient for total packs to be vanishingly small (10^{-4}), and this variable was removed from the analysis.

29. Lewis, B.M., Pitfalls of spirometry, J. Occup. Med. 23: 35-38, 1981.

Findings on medical history or reported symptomatology thought to be relevant to the spirometric variables were coded 0 for absent and 1 for present. Chest x-ray findings were coded 0 for normal and 1 for abnormal. Respiratory and cardiovascular findings were not distinguished.

In the analysis age and service time were found to be colinear in the population ($r = 0.73$) and we have used age as the independent variable.

Results

Table 14.1 gives the mean values and standard deviations for the variables in this study. Missing data are shown by the N-value. The females were somewhat older and had lower homolog serum values that were somewhat higher, but their mean service time was comparable to the males. The elevated serum PCB levels in females relate to their employment as capacitor sealers and in salvage and repair, jobs with relatively high dermal exposure levels.

Smokers and ex-smokers constituted 73 and 59 percent of the male and female population respectively. Males on the average smoked more packs per day (1.38) than females (1.15), but females had smoked for a longer time so that total consumption was comparable. When nonsmokers are included the males as a group were the heaviest smokers and averaged 1 pack per day for 14 years.

Nearly 50 percent of the population had some relevant medical history or symptomatology but only 7.5 percent of females and 9.0 percent

Table 14.1. Mean values and standard deviations for pulmonary function and associated variables in PCB-exposed capacitor workers (Group 1). Males and females tabulated separately. Smoking code: non-smokers (1); ex-smokers (2); and smokers (3). Relevant history and x-ray findings coded 0 = absent, 1 = present. FEV_1/FVC as percent of predicted calculated from population mean age and height; others calculated individually. Geometric means for PCB level as ppb in brackets.

	Males				Females			
	$\bar{X}$	S.D	N		$\bar{X}$	S.D	N	
Age (years)	43.04	11.08	146		50.39	10.89	41	
Service (years)	13.76	9.13	146		13.98	8.41	41	
Height (cms)	175.49	7.16	146		159.90	5.33	41	
Weight (kgs)	80.49	12.46	132		62.08	10.98	38	
Smoking (Total Population)								
Smoking Code	2.15	0.879	146		2.02	0.935	41	
No. Packs/Year	369.13	287.7	146		246.15	249.07	41	
No. Years Smoked	13.97	12.12	146		13.39	14.15	41	
Total Packs	7336.25	7990.31	146		5922.35	7029.83	41	
Smokers and Ex-Smokers								
No. Packs/Year	503.67	211.75	107		420.51	177.14	24	
No. Years Smoked	18.72	10.38	109		22.88	11.03	24	
Total Packs	10,104.65	7741.25	106		10,117.34	6454.27	24	
Relevant Med. History	0.472	0.506	146		0.493	0.512	41	
Chest X-Ray	0.0897	0.287	145		0.0750	0.267	40	
FVC	4.96	0.930	146		3.14	0.874	41	
FVC (% of Predicted)	105.29	14.27	146		100.76	20.83	41	
FEV_1	3.80	0.841	146		2.33	0.683	41	
FEV_1 (% of Predicted)	100.95	17.55	146		91.24	19.10	41	
$FEV_1/FVC \times 100$	76.62	9.16	146		73.93	9.61	41	
FEV_1/FVC (Predicted)	82.35				89.63			
Log PCB (lower homologs)	2.41	0.483	132	(257)	2.59	0.375	37	(389)
Log PCB (higher homologs)	1.57	0.451	112	(37)	1.45	0.417	28	(28)

of males had positive x-ray findings.

For the population as a whole FVC and FEV_1 average values were comparable to the Knudson standards. FEV_1/FVC values are low with respect to the Knudson standard calculated using the average age and height of the male and female groups.

In Table 14.2 the prevalence of clinical conditions and symptomatology relevant to spirometry are tabulated. Seventy-nine individuals (42 percent) had one or more complaints or medical history related to the respiratory tract or the cardiovascular system. The predominant finding was a high prevalence of chronic upper and lower respiratory tract infection. Leukoplakia and vocal cord polyps were found in heavy smokers. On x-ray examination (Table 14.3) pulmonary scarring, calcification, granulomas, and other evidence of old pulmonary infection was found in 12 subjects and emphysema suspected in six in whom blebs were identified in 3 cases. A coin lesion was found during the course of this study which proved to be malignant.

The prevalence of abnormal spirometric findings are shown in Table 14.4. Abnormal findings occurred primarily in smokers and ex-smokers and were more than twice as high in females who smoked for a longer period. Ten subjects (5.3 percent) showed a reduced vital capacity compared to the 14 percent reported by Warshaw et al. (24) for the less heavily exposed group. The one predominant finding was an abnormally low value for FEV_1/FVC ($\leq$70 percent) which occurred primarily in smokers. Using the criteria of $\leq$75 percent for FEV_1/FVC 38.5 percent were low including sixteen nonsmokers.

Table 14.2. Respiratory and cardiovascular conditions in the medical history of PCB-exposed capacitor workers (Group 1). Note occurrence of leukoplakia and laryngeal polyps.

Upper Respiratory Tract			62
Allergy		17	
Hay Fever	6		
Asthma	2		
Other	9		
Sinusitis		24	
Chronic Tonsillitis		2	
Frequent URI		6	
Leukoplakia and polyps, larynx, throat		4	
Septoplasty		7	
Fracture, nose		2	
Lower Respiratory Tract			47
Chronic Bronchitis		12	
Emphysema		7	
Pneumonia (episodes)		11	
Lung Infections (unspecified)		3	
Pleurisy		2	
Healed tuberculosis		1	
Pulmonary fibrosis		1	
Carcinoma of lung		2	
Thoracic arthritis		1	
Fracture, ribs		5	
Contused lung	2		
SOB, cough, sputum		2	
Cardiovascular Systems			30
Hypertension		18	
Coronary insufficiency		7	
Atrial tachycardia		1	
Rheumatic fever		3	
Carotid endarterectomy		1	
			139

Table 14.3. Chest x-ray findings during medical examination of PCB-exposed capacitor workers. The coin lesion discovered at this examination proved malignant.

Emphysema	6
Blebs 3	
Chronic pul. infection and tiny calcification	5
Adhesions, costophrenic angle	3
Pleural thickening	2
Calcified granuloma	2
Pul. scar	2
Coin lesion	1
Atherosclerosis, Aorta	2
Cardiomegaly	1
Scoliosis	1
	25

Table 14.4. Prevalence of spirometric abnormalities in 187 PCB-exposed capacitor workers (Group I). Criteria for abnormality of FEV_1/FVC given as percent of predicted using standards of Knudson et al. (<70%) compared to the older standard (<75%) used by Warshaw et al.

	Male			Female		
	Non-Smokers	Current & Ex-smokers	All	Non-Smokers	Current & Ex-smokers	All
FVC*	0/41	5/105(4.8%)	5/146(3.4%)	1/15(0.7%)	4/26(15.4%)	5/41(12.2%)
FEV_1*	0/41	11/105(10.5)	11/146(7.5%)	0/15	8/26(30.8%)	8/41(19.5%)
FEV_1/FVC+	0/41	21/105(20.0%)	21/146(14.4%)	1/15(0.7%)	11/26(42.3%)	12/41(29.3%)
++	12/41/29.3%)	36/105(34.3%)	48/146(32.9%)	4/15(26.7%)	20/26(76.9%)	24/41(58.5%)

* ≤ 79.5%
\+ < 70.0%
++ < 75.0%

Spirometric patterns were categorized according to the criteria shown in Table 14.5. Of the ten subjects showing a reduced forced vital capacity (Table 14.4), four were the cases of chronic obstructive lung disease. The balance averaged 15 kgs (2-28 kgs) over the maximum desirable weight for their height and frame. The four subjects showing a restrictive pat ern were between 8 and 21 kgs overweight by this standard. An obstructive pattern was found in 23 subjects, primarily smokers and ex-smokers.

Regression Analysis

Multiple linear regression analyses were performed for the total population with FVC, FEV_1 and FEV_1/FVC as the dependent variables, and sex as an independent variable. For forward stepwise regression the criteria for adding a variable was an F-ratio of 3.0 ($F_{1,\infty}(3.84)=0.95$). Table 14.6 shows the estimated coefficients, their standard errors and the statistics of the fitted equation for the stepwise regressions. They show the expected dependence on sex, height and age for FVC and FEV_1. For the population there is a significant association with the duration of smoking rather than the smoking rate (packs/year) or total packs. There is also an association with medical history and symptomatology and FEV_1, and between positive x-ray findings and FEV_1/FVC.

Omission of the serum PCB levels increased the number of subjects for analysis and strengthened the observed relations (Table 14.7). In particular a significant negative relation between body weight and the FVC was found. Separate studies showed this relation held for males but not females. The multiple correlation coefficient (R) for FEV_1/FVC

Table 14.5. Spirometric patterns (restrictive, obstructive, mixed) observed in 187 PCB-exposed capacitor workers (Group 1). Using the $FEV_1/FVC > 70\%$ criteria a restrictive pattern was seen in only 2.1 percent of workers.

Type	Criteria	Males	Females	All
Restrictive	$FVC < 79.5$; $FEV_1 < 79.5$ $FEV_1/FVC > 70$	2	2	4 (2.1%)
Obstructive	$FVC > 79.5$; $FEV_1/FVC < 70$	14	9	23 (12.3%)
Mixed	$FVC < 79.5$; $FEV_1 < 79.5$; $FEV_1/FVC < 70.0$	2	2	4 (2.1%)
		18 (9.6%)	13 7.0%	31 (16.6%)

Table 14.6. Multiple stepwise linear regression study of spirometric variables in PCB-exposed capacitor workers (Group 1). FVC, FEV_1 and FEV_1/FVC were dependent variables. Serum PCB levels (as Aroclor 1242 and 1260) were independent variables. Outliers have been omitted: N = 137. No association was found with serum PCB levels.

Variable	FVC			FEV_1			FEV_1/FVC		
	Est.C.	S.E.	F-Ratio	Est.C.	S.E.	F-Ratio	Est.C.	S.E.	F-Ratio
Height, cms	0.048	0.008	34.12	0.030	0.007	17.96	-	-	-
Age, years	-0.019	0.007	7.51	-0.023	0.006	17.29	-	-	-
Sex	-0.817	0.192	18.03	-0.778	0.164	22.52	-3.18	1.61	3.92
Years of Smoking	-0.029	0.007	15.26	-0.018	0.005	14.68	-0.12	0.055	4.69
Relevant History	-	-	-	-0.249	0.104	5.76	-	-	-
X-Ray Positive	-	-	-	-	-	-	-7.47	2.40	9.70
Intercept	-1.19	1.67	-	0.657	1.41	-	83.10	2.24	-

Statistics of Fitted Equation	FVC	FEV_1	FEV_1/FVC
F-Ratio	38.16	43.64	7.70
S.D.	0.671	0.578	7.55
R	0.799	0.790	0.435
R^2	63.78%	62.49%	18.93%

Table 14.7. Same as Table 14.6 except serum PCB levels eliminated as independent variables. Note the significant negative association of body weight and FVC. N = 165.

Variable	FVC			FEV_1			FEV_1/FVC		
	Est.C.	S.E.	F-Ratio	Est.C.	S.E.	F-Ratio	Est.C.	S.E.	F-Ratio
Height, cms	0.060	0.008	51.44	0.032	0.007	23.70	-	-	-
Age, years	-0.026	0.005	23.96	-0.026	0.005	32.90	-	-	-
Sex	-0.862	0.172	24.59	-0.787	0.147	28.67	-3.51	1.44	5.96
Years of Smoking	-0.016	0.005	12.33	-0.015	0.004	14.31	-0.136	0.050	7.48
Relevant History	-	-	-	-0.225	0.092	5.97	-	-	-
X-Ray Positive	-	-	-	-	-	-	-8.84	2.33	14.41
Body Weight, kgs	-0.010	0.005	4.22	-	-	-	-	-	-
Intercept	2.51	1.52		0.402	1.31		83.07	1.98	

Statistics of Fitted Equation	FVC	FEV_1	FEV_1/FVC
F-Ratio	66.35	63.90	10.65
S.D.	0.656	0.564	7.62
R	0.822	0.817	0.407
R^2	67.59%	66.77%	16.56%

appears low but is the same order of magnitude as found by Knudson et al. in his normal population.

In male nonsmokers for which serum PCB levels were available (N=33) regression showed a significant positive relation between FVC and the lower PCB homologs (Aroclor 1242) which represented the only statistically significant relation found among serum PCB levels and the spirometric variables (Table 14.8). For females and for subgroups of males involving small numbers of subjects the regression equations were of marginal statistical significance. For example, for the males there were weak associations found between the hematocrit and FVC ($F_{1,128}$=5.29) and the PMN leukocyte count and FEV_1/FVC ($F_{1,128}$=5.62) suggestive of early hypoxia in the former case and an infectious element in the latter. Although the F-ratios were significant, the multiple correlation coefficients were not (R^2=4-5 percent).

For the regression equations employing raw data, examination of the residuals showed them to be normally distributed. Regression using the values as percent of predicted values showed residuals that were not normally distributed and yielded equations of uncertain statistical significance.

Discussion

A substantial series of linear regression equations have been proposed relating FVC, FEV_1 and their ratio to height and age in large groups of asymptomatic nonsmokers. The coefficients of our prediction equations (when separated by sex) agreed most closely with those

Table 14.8. Same as Table 14.6 except only male non-smokers included (N = 33). FVC is the dependent variable. Note that significant positive association between FVC and serum L-PCB.

	Coeff	S.E.	F-Ratio
Intercept	-2.63	1.89	-
Age (yrs)	-0.031	0.006	27.8
Height (cms)	0.046	0.010	21.4
L-PCB	0.272	0.121	5.1

Statistics of Fit

F-Ratio	19.4
S.D.	0.382
R	0.817
R^2	66.7%

of Ferris et al. (30), who included smokers and ex-smokers in their population. In our results the 95 percent confidence limits of the coefficients were quite large; thus, the use of the Knudson et al. standards to normalize the data for each sex appeared to be generally effective. The agreement with Knudson et al. is somewhat surprising in view of the medical and smoking histories, the limited number of subjects and the field nature of the data as compared to the careful observations of Knudson in asymptomatic nonsmokers.

The regression studies identified the number of years smoked as a significant variable rather than smoking rate (packs/year) or the total packs smoked. This is at variance with MacIntyre et al. (31), who found in a longitudinal study of 1,000 male Naval aviators, that the duration of smoking was more important for residual volume measurements whereas total packs were more important for vital capacity measurements. In their study the residual volume increases and the vital capacity decreases seemed to balance each other so that their sum, the total lung capacity, was only minimally related to smoking.

Body weight was shown to be a significant variable in males for FVC in our population. This inverse relation was also found by MacIntyre et al. Apparently excess weight tends to diminish diaphragmatic and chest wall excursion. The effect is seen both for baseline weight and weight change according to MacIntyre et al. This factor

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30. Ferris, B.G., J., Anderson, D.O. and R. Zickmantel. Prediction values for screening tests of pulmonary function. Am. Rev. Resp. Dis. 91: 252, 1965.

31. MacIntyre, N.R., Mitchell, R.E., Oberman, A. et al. Long-term follow-up of lung volume measurements in initially healthy young aviators. Avia Space Envir. Med. 52: 1-5, 1981.

appears to account for the prevalence of reduced FVC in our population. The prevalence (5.3 percent) was equivalent to that found for styrene and PVC-exposed workers (24).

Obesity may also account for the significant positive relation between serum Aroclor 1242 level and FVC found in nonsmokers, which might suggest a pulmonary benefit from PCB exposure. However, there is an inverse relation between body weight and serum PCB level, which is particularly apparent in starvation (32). For a constant PCB body burden weight gain or loss results in the redistribution of PCBS in the body lipid stores, so that generally higher serum PCB levels are found in individuals with the lowered body fat content. Thus, as body weight increases, both FVC and serum PCB levels should tend to decline together, and hence appear to be related. No other formal relation between PCB exposure and spirometric variables was found.

Obstructive defects, as evidenced by reduced FEV_1 and FEV_1/FVC values, represented a principal finding in this population. Four individuals were frank emphysemics. Eighteen percent of subjects had FEV_1/FVC values <70 percent of predicted and 38.5 percent had FEV_1/FVC values less than 75 percent of predicted. This latter value is equivalent to the findings of Lorimer et al. (33) in styrene workers using the 75 percent criterion.

32. Hesselberg, R.J. and D.D. Sherr. PCB's and p,p'-DDE in the blood of cachectic patients. Bull. Environ. Contam. Toxicol. 11: 02-205, 1974.

33. Lorimer, M.V., Lilis, R., Nicholson, W.J., et al. Clinical studies of styrene workers: Initial findings. Environ. Health Persp. 17: 171-181, 1976.

The mortality rate for emphysema (492, 8th Rev. ICD) has been substantially higher in rural upstate New York, where these plants are located, as compared to more urban areas (34). This rural-urban gradient is not unique to New York State and pulmonary emphysema and chronic bronchitis not a universally urban disease as proposed by Mano (35). For instance, Hammond (36) found that among men, both with and without occupational exposure to a variety of agents an for each smoking category, indications of emphysema were more common among rural than among metropolitan residents. It is reported (37) that mortality rates for chronic respiratory disease up to 1968 were lowest in the middle Atlantic region (New York, New Jersey, Pennsylvania) and highest in the mountain region (Montana, Idaho, Wyoming, etc.), a finding which does not suggest correlation with factors such as environmental pollution and urbanization. In contrast, lung cancer mortality in upstate New York has been shown to be a function of urbanization as measured by population density (38).

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34. Rubin, B.B., Mortality from lung cancer, emphysema and bronchitis for counties in New York State, excluding New York City, 1960-1975. New York State Department of Health Monograph No. 16, Albany, NY, Oct. 1980.

35. Mano, N.E., Comparative mortality among metropolitan areas of the United States: 1949-1951; 102 Causes of Death. Public Health Service Pub., No. 562, 1957.

36. Hammond, E.C., and Selikoff, I.J., The effects of air pollution; epidemiological evidence. In: Pheumoconiosis. Proc. Int. Conf. Johannesburg 1969. Ed. H.A. Shapiro. Oxford University Press, 1970. p. 368-373.

37. Stat. Bull. Metrop. Life Ins. Co. July 1973.

38. Nasca, P.C., Burnett, W.S., Greenwald, P., et al. Population density as an indicator of urban-rural differences in cancer incidence, upstate New York, 1968-1972. Am. J. Epidemiol. 112: 362-375, 1980.

The population of this study was drawn from two primarily rural counties and one county classified as urban. This mixed demography is complicated by the presence of other established occupational carcinogens in the area. The second largest employer in the region has been a paint pigment manufacturer where chromate exposure and the ensuing nasal septal perforation and carcinoma of the lung has been occasionally seen in older employees. Prior work histories of the lung cancer deaths of the Brown study are not currently available, but of the three deaths which have occurred since 1976 in the present study population, two were due to adenocarcinoma of the lung, both in heavy smokers, of whom one was in an individual formerly employed by the pigment manufacturer. In view of the diversity of occupational exposures experienced by our study group (Table 14.9) prior to employment in capacitor manufacturing, such data should be treated with caution.

Macklem and Kilburn (39) have reviewed the pathophysiology of chronic obstructive lung disease and pulmonary neoplasia, particularly with respect to environmental factors. Over 150 environmental agents have been identified which are associated with pulmonary fibrosis in which the agents are generally pulmonary irritants. There is no evidence in the literature, or in our experience over 33 years of plant operation, that PCBs act as an acute pulmonary irritant. Cigarette smoking, however, is firmly implicated as a part of the etiological pattern in chronic obstructive lung disease and respiratory malignancy, as a major pulmonary irritant in the former case and as a synergistic agent in the case of malignancy (36).

39. Macklem, P., and Kilburn, K.H., Tracheobronchial response to insult. In: Environmental Factors in Respiratory Disease. Ed. D.H.K. Lee Academic Press, New York 1972. p. 31.

Table 14.9. Potential exposure to respiratory agents in prior employment from review of available employment applications.

Chromate dust and paint pigment	12
Other chemicals and pesticides (farmers, gas station attendants, laboratory personnel, etc.)	22
Lint (shirt, carpet and other factories)	10
Mining, cement, and stone	10
Asbestos (pipefitters, plumbers, electricians, construction)	23
Heavy metals and foundry	10
Military Service – Possible multiple exposures	35
Paper mills	8

The present study provides no direct evidence that PCB exposure, as measured by serum PCB levels, is correlated with the occurrence of spirometric abnormalities. The prevalence of restrictive patterns in PCB workers previously reported has not been confirmed. The prevalence of chronic respiratory disease and the occurrence of carcinoma of the lung in this population appear most likely to be coupled to heavy smoking, the possibility of chromate exposure and demographic factors.

CERTIFICATE OF AUTHENTICITY

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